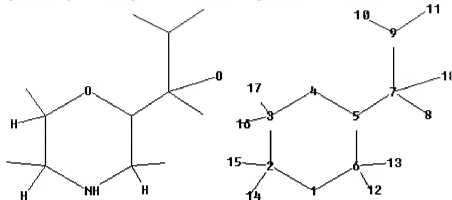


<http://www.cas.org/support/stngen/stdoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10581015_1.str



chain nodes :

7 8 9 10 11 12 13 14 15 16 17 18

ring nodes :

1 2 3 4 5 6

chain bonds :

2-14 2-15 3-16 3-17 5-7 6-12 6-13 7-8 7-9 7-18 9-10 9-11

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-18

exact bonds :

2-14 2-15 3-16 3-17 5-7 6-12 6-13 7-8 7-9 9-10 9-11

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS

9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS

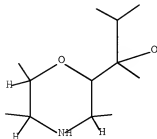
16:CLASS 17:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s ll sss sam

SAMPLE SEARCH INITIATED 09:46:27 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 0

ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 33 TO 447

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s ll sss full

FULL SEARCH INITIATED 09:46:34 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 233 TO ITERATE

100.0% PROCESSED 233 ITERATIONS 0

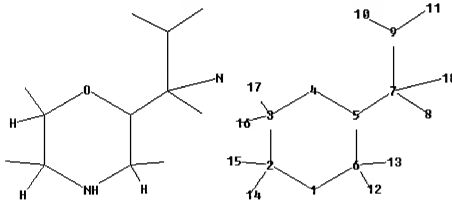
ANSWERS

SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=>

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chain nodes :

7 8 9 10 11 12 13 14 15 16 17 18

ring nodes :

1 2 3 4 5 6

chain bonds :

2-14 2-15 3-16 3-17 5-7 6-12 6-13 7-8 7-9 7-18 9-10 9-11

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-18
exact bonds :
2-14 2-15 3-16 3-17 5-7 6-12 6-13 7-8 7-9 9-10 9-11

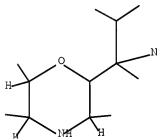
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS
9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS
16:CLASS 17:CLASS 18:CLASS

L4 STRUCTURE UPLOADED

=> d l4

L4 HAS NO ANSWERS

L4 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l5 sss sam

L5 NOT FOUND

The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l4 sss full

FULL SEARCH INITIATED 09:47:37 FILE 'REGISTRY'

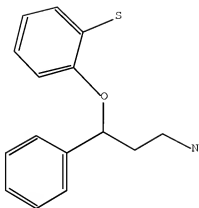
FULL SCREEN SEARCH COMPLETED - 358 TO ITERATE

100.0% PROCESSED 358 ITERATIONS 0
ANSWERS
SEARCH TIME: 00.00.01

L5 0 SEA SSS FUL L4

=>

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Structure attributes must be viewed using STN Express query preparation.

=> s l6 sss sam

SAMPLE SEARCH INITIATED 09:48:05 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 11 TO ITERATE

100.0% PROCESSED 11 ITERATIONS

3

ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 22 TO 418

PROJECTED ANSWERS: 3 TO 163

L7 3 SEA SSS SAM L6

=> s l6 sss full

FULL SEARCH INITIATED 09:48:11 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 145 TO ITERATE

100.0% PROCESSED 145 ITERATIONS

24

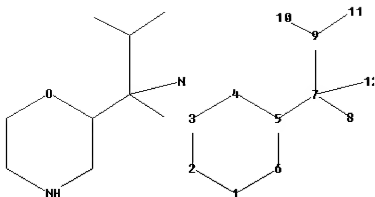
ANSWERS

SEARCH TIME: 00.00.01

L8 24 SEA SSS FUL L6

=>

Uploading C:\Program Files\Stnexp\Queries\10581015_5.str



```

chain nodes :
7 8 9 10 11 12
ring nodes :
1 2 3 4 5 6
chain bonds :
5-7 7-8 7-9 7-12 9-10 9-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-12
exact bonds :
5-7 7-8 7-9 9-10 9-11

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS
9:CLASS 10:CLASS 11:CLASS 12:CLASS

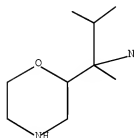
```

L9 STRUCTURE UPLOADED

=> d l9

L9 HAS NO ANSWERS

L9 STR



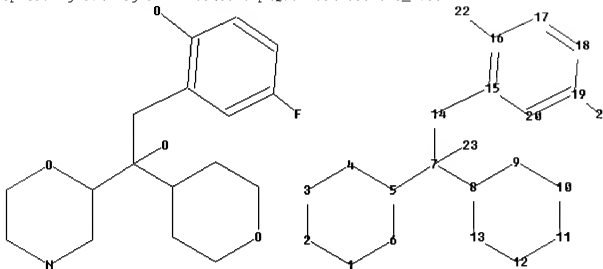
Structure attributes must be viewed using STN Express query preparation.

```
=> s 19 sss full
FULL SEARCH INITIATED 09:49:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      181 TO ITERATE
```

```
100.0% PROCESSED      181 ITERATIONS      0
ANSWERS
SEARCH TIME: 00.00.01
```

```
L10      0 SEA SSS FUL L9
```

```
=>
Uploading C:\Program Files\Stnexp\Queries\10581015_4.str
```



```
chain nodes :
7 14 21 22 23
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 13 15 16 17 18 19 20
chain bonds :
5-7 7-8 7-14 7-23 14-15 16-22 19-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13 15-
16 15-20 16-17 17-18 18-19 19-20
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-23 8-9 8-13 9-10 10-11 11-12 12-
13 16-22
exact bonds :
5-7 7-8 7-14 14-15 19-21
normalized bonds :
15-16 15-20 16-17 17-18 18-19 19-20
```

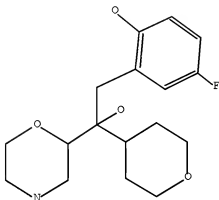
```
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:CLASS 15:Atom 16:Atom 17:Atom
18:Atom 19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS
```

L11 STRUCTURE UPLOADED

=> d l11

L11 HAS NO ANSWERS

L11 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l11

SAMPLE SEARCH INITIATED 09:50:28 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0
ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L12 0 SEA SSS SAM L11

=> s l11 sss full

FULL SEARCH INITIATED 09:50:37 FILE 'REGISTRY'

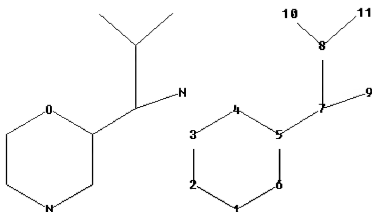
FULL SCREEN SEARCH COMPLETED - 34 TO ITERATE

100.0% PROCESSED 34 ITERATIONS 8
ANSWERS
SEARCH TIME: 00.00.01

L13 8 SEA SSS FUL L11

=>

Uploading C:\Program Files\Stnexp\Queries\10581015_6.str



```

chain nodes :
7 8 9 10 11
ring nodes :
1 2 3 4 5 6
chain bonds :
5-7 7-8 7-9 8-10 8-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-9
exact bonds :
5-7 7-8 8-10 8-11

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS
9:CLASS 10:CLASS 11:CLASS

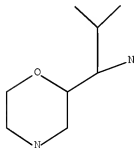
```

L14 STRUCTURE UPLOADED

=> d l14

L14 HAS NO ANSWERS

L14 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l14 sss sam

SAMPLE SEARCH INITIATED 09:53:04 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 72 TO ITERATE

100.0% PROCESSED 72 ITERATIONS 1
ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 931 TO 1949
PROJECTED ANSWERS: 1 TO 80

L15 1 SEA SSS SAM L14

=> s l14 sss full

FULL SEARCH INITIATED 09:53:10 FILE 'REGISTRY'

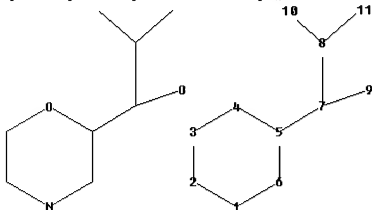
FULL SCREEN SEARCH COMPLETED - 2022 TO ITERATE

100.0% PROCESSED 2022 ITERATIONS 6
ANSWERS
SEARCH TIME: 00.00.01

L16 6 SEA SSS FUL L14

=>

Uploading C:\Program Files\Stnexp\Queries\10581015_7.str



chain nodes :
7 8 9 10 11
ring nodes :
1 2 3 4 5 6
chain bonds :
5-7 7-8 7-9 8-10 8-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-9
exact bonds :

5-7 7-8 8-10 8-11

Match level :

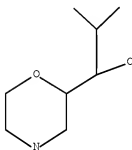
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS
9:CLASS 10:CLASS 11:CLASS

L17 STRUCTURE UPLOADED

=> d l17

L17 HAS NO ANSWERS

L17 STR



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l16 and l18

2 L16

10 L18

L19 0 L16 AND L18

=> s l16

L20 2 L16

=> d l20 ibib abs

L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:114255 CAPLUS Full-text

DOCUMENT NUMBER: 138:287603

TITLE: Amino Acid-Derived Heterocycles as
Combinatorial

AUTHOR(S):
CORPORATE SOURCE: Library Targets: Spirocyclic Ketal Lactones
Trump, Ryan P.; Bartlett, Paul A.
Center for New Directions in Organic
Synthesis,
Department of Chemistry, University of

California,

SOURCE: Berkeley, CA, 94720-1460, USA
Journal of Combinatorial Chemistry (2003),

5(3),

285-291

CODEN: JCCHFF; ISSN: 1520-4766

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

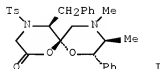
LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 138:287603

GI



AB The spirocyclic ketal-lactone frameworks, e.g., I, were designed as novel structures amenable to combinatorial synthesis. The synthesis of representative analogs was developed in solution and on solid support, the scope of effective input materials was determined, and the stability and stereochem. of the products was evaluated. The spirocycles are obtained in modest overall yields (5-36%) and excellent purities (>72%) and offer a promising motif for combinatorial prospecting libraries.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

=> d 120 ibib abs 1-2

L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:114255 CAPLUS Full-text

DOCUMENT NUMBER: 138:287603

TITLE: Amino Acid-Derived Heterocycles as Combinatorial

Library Targets: Spirocyclic Ketal Lactones

AUTHOR(S): Trump, Ryan P.; Bartlett, Paul A.

CORPORATE SOURCE: Center for New Directions in Organic Synthesis,

Department of Chemistry, University of

California,

Berkeley, CA, 94720-1460, USA

SOURCE: Journal of Combinatorial Chemistry (2003), 5(3),

285-291

CODEN: JCCHFF; ISSN: 1520-4766

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

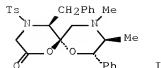
LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 138:287603

GI



AB The spirocyclic ketal-lactone frameworks, e.g., I, were designed as novel structures amenable to combinatorial synthesis. The synthesis of representative analogs was developed in solution and on solid support, the scope of effective input materials was determined, and the stability and stereochem. of the products was evaluated. The spirocycles are obtained in modest overall yields (5-36%) and excellent purities (>72%) and offer a promising motif for combinatorial prospecting libraries.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:332763 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 137:63471

TITLE: Synthesis and Pharmacological Evaluation of an Analogue of the Peptide Hormone Oxytocin That

Contains

a Mimetic of an Inverse γ -Turn

AUTHOR(S): Yuan, ZhongQing; Blomberg, David; Sethson, Ingmar;

Brickmann, Kay; Ekholm, Kjell; Johansson,

Birgitta;

Nilsson, Anders; Kihlberg, Jan

CORPORATE SOURCE: Organic Chemistry, Department of Chemistry, Umea

University, Umea, SE-901 87, Swed.

SOURCE: Journal of Medicinal Chemistry (2002), 45(12), 2512-2519

CODEN: JMCMAR; ISSN: 0022-2623

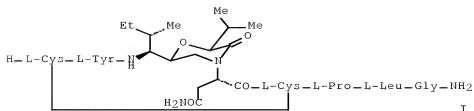
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:63471

GI



AB Oxytocin is a neurohypophyseal peptide hormone that induces labor and lactation in mammals. Cyclic peptide I, an oxytocin analog containing the inverse γ -turn mimetic composed of tripeptide Ile-Val-Asn in place of residues Ile3-Gln4-Asn5 in oxytocin, has been synthesized to probe the hypothesis that a γ -turn involving these residues is found in the receptor bound conformation of oxytocin. In the turn mimetic, residues i and i + 1 are connected by a ψ [CH2O] isostere while a covalent methylene bridge replaces the hydrogen bond that is often found between residues i and i + 2 in γ -turns. The turn mimetic was assembled from three types of building blocks: an azido epoxide, an α -bromo acid, and a protected β -amino alc. I did not induce contractions of the uterus nor did it inhibit oxytocin-induced contractions. It is suggested that the loss of bioactivity of I is mainly due to the presence of a ψ [CH2O] isostere instead of an amide bond between residues i and i + 1 in the turn mimetic.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE

=> s 118

L21 10 L18

=> d 121 ibib abs 1-10

L21 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1176480 CAPLUS Full-text

DOCUMENT NUMBER: 143:440426

TITLE: Substituted morpholine compounds for the treatment of

preparation central nervous system disorders, their

and pharmaceutical compositions

INVENTOR(S): Barta, Nancy S.; Glase, Shelly Ann; Gray, David L.;

Reichard, Gregory A.; Simons, Lloyd J.; Xu,

Weijan

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: U.S. Pat. Appl. Publ., 85 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050245519	A1	20051103	US 2005-119210	
20050429				
AU 2005238296	A1	20051110	AU 2005-238296	
20050419				
CA 2564994	A1	20051110	CA 2005-2564994	
20050419				
WO 2005105763	A1	20051110	WO 2005-1B1158	
20050419				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1745029	A1	20070124	EP 2005-733459	
20050419				
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1950348	A	20070418	CN 2005-80013776	
20050419				
BR 2005010453	A	20071030	BR 2005-10453	
20050419				
JP 2007535530	T	20071206	JP 2007-510153	
20050419				
JP 4185154	B2	20081126		
NL 1028924	A1	20051101	NL 2005-1028924	
20050429				
NL 1028924	C2	20060427		
IN 2006DN05782	A	20070803	IN 2006-DN5782	
20061005				
MX 2006012505	A	20061215	MX 2006-12505	
20061027				

KR 2007006881	A	20070111	KR 2006-722767	
20061030				
NO 2006005456	A	20070104	NO 2006-5456	
20061127				
JP 2008019267	A	20080131	JP 2007-233201	
20070907				
PRIORITY APPLN. INFO.:			US 2004-567244P	P
20040430				
			JP 2007-510153	A3
20050419			WO 2005-IB1158	W
20050419				
OTHER SOURCE(S):		CASREACT 143:440426; MARPAT 143:440426		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. of the formula I, which can be used in the treatment of central nervous system disorders. In compds. I, A is O or S; X is C1-10 alkyl, C2-8 alkenyl, aryl, heterocyclyl, C1-6 alkoxy, etc., with each group optionally substituted; and R1 - R5 are independently selected from H, OH, halo, C1-6 alkyl, aryl, C3-8 cycloalkyl, C2-6 alkenyl, C1-6 alkoxy, aryloxy, heterocyclyl, etc.; including pharmaceutically acceptable salts, enantiomers and diastereomers. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of central nervous system disorders. Ring opening of (R,R)-phenylglycidol with 1-naphthol followed by silylation of the primary alc., mesylation of the secondary alc., and desilylation gave mesylate II, which underwent ring closure to the epoxide, ring opening with ammonium hydroxide and amidation with chloroacetyl chloride, resulting in the formation of amide III. Compound III was converted to the morpholine by intramol. cyclization and Red-Al reduction to give morpholine IV. Several compds., e.g., IV, express high inhibition of human norepinephrine transporter (hNET) and human serotonin transporter (hSERT).

L21 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:588645 CAPLUS Full-text
 DOCUMENT NUMBER: 143:115550
 TITLE: Preparation of heterocyclic compounds as selective
 norepinephrine reuptake inhibitors for
 treating hot flashes, impulse control disorders and
 personality change due to a general medical condition
 INVENTOR(S): Allen, Albert John; Hemrick-Luecke, Susan;
 Sumner, Calvin Russell; Wallace, Owen Brendan

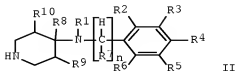
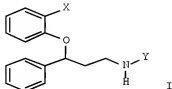
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 337 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005060949	A2	20050707	WO 2004-US38221	
20041201				
WO 2005060949	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2548304	A1	20050707	CA 2004-2548304	
20041201				
EP 1729754	A2	20061213	EP 2004-811076	
20041201				
EP 1729754	B1	20080702		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1889940	A	20070103	CN 2004-80036841	
20041201				
JP 2007513945	T	20070531	JP 2006-543830	
20041201				
AT 399557	T	20080715	AT 2004-811076	
20041201				
ES 2307071	T3	20081116	ES 2004-811076	
20041201				
US 20070015786	A1	20070118	US 2006-581015	
20060530				
KR 2006121178	A	20061128	KR 2006-711571	
20060612				
PRIORITY APPLN. INFO.:			US 2003-529428P	P
20031212				

20041201

OTHER SOURCE(S):
GI

CASREACT 143:115550; MARPAT 143:115550



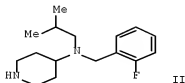
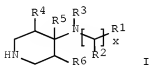
AB The invention relates to a method of preventing or treating hot flashes, vasomotor symptoms, impulse control disorders or personality change due to a general medical condition, comprising administering to a patient in need thereof a therapeutically effective amount of a selective norepinephrine reuptake inhibitor selected from atomoxetine, reboxetine, I [X = alkylthio; Y = alkyl], II [n = 1-3; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2-R4 = H, alkyl, alkoxy, etc.; R5-R6 = H, alkyl, alkoxy, halo; R7-R8 = H, alkyl; R9-R10 = H, halo, OH, CN, alkyl, alkoxy], etc. Over 200 title compds. such as I, II and other heterocyclic compds. disclosed, were prepared E.g., a 2-step synthesis of N-(2-methylpropyl)-N-[(2-fluorophenyl)methyl]piperidin-4-amine fumarate, starting from tert-Bu 4-(2-methylpropylamino)piperidine-1-carboxylate and 2-fluorobenzaldehyde, was given. The preferred exemplified title compds. exhibit a Ki value less than 1 μ M, more preferably less than 500 nM at the norepinephrine transporter as determined using the scintillation proximity assay.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:523264 CAPLUS Full-text
 DOCUMENT NUMBER: 143:59831
 TITLE: A preparation of aminopiperidine derivatives, useful for the treatment of cognitive failure
 INVENTOR(S): Hatfield, Alan Kramer; Bymaster, Franklin
 Porter;
 McKinzie, David Lee; Tucker, Tina Marie;
 Keaffaber, Kirk Matthew; Sumner, Calvin Russell;
 Trzepacz, Paula Terese; Allen, Albert John; Kelsey, Douglas
 Kenneth; Michelson, David; Gehlert, Donald Richard;
 Yang, Charles Renkin
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 300 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053663	A2	20050616	WO 2004-US37195	
20041124				
WO 2005053663	A3	20050811		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2003-524450P	P
20031124			US 2003-524781P	P
20031125				
OTHER SOURCE(S):		MARPAT 143:59831		
GI				



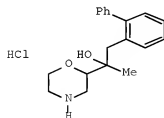
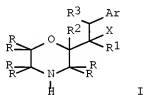
AB The invention relates to a preparation of aminopiperidine derivs. of formula I [wherein: x is 1-3; R1 is (un)substituted phenyl; R2 and R5 are independently H or alkyl; R3 is (cyclo)alkyl, alkenyl, or cycloalkylalkyl, etc.; R4 is H, halogen, or OH, etc.; R6 is H,

halogen, CN, or alkyl, etc.], useful for the treatment of cognitive failure. Selective norepinephrine reuptake inhibitors were used to treat cognitive failure. For instance, fumarate salt of aminopiperidine derivative II was prepared via imination of 2-fluorobenzaldehyde by tert-Bu 4-[(2-methylpropyl)amino]piperidine-1-carboxylate, reduction of the obtained imine, and subsequent fumaric acid salt formation. The preferred invention compds. exhibit Ki values less than 500 nM at the norepinephrine transporter.

L21 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:451370 CAPLUS Full-text
 DOCUMENT NUMBER: 142:482071
 TITLE: Preparation of morpholine derivatives as norepinephrine reuptake inhibitors
 INVENTOR(S): Campbell, Gordon Iain; Cases-Thomas, Manuel Javier;
 Man, Teresa; Masters, John Joseph; Rudyk, Helene
 PATENT ASSIGNEE(S): Catherine Eugenie; Walter, Magnus Wilhelm
 SOURCE: Eli Lilly and Company, USA
 PCT Int. Appl., 133 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005047272	A1	20050526	WO 2004-US32771	
20041028				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004289616	A1	20050526	AU 2004-289616	
20041028				

CA 2544649	A1	20050526	CA 2004-2544649
20041028			
EP 1682523	A1	20060726	EP 2004-794209
20041028			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,			
MC, PT,			
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,			
PL, SK, HR			
CN 1878762	A	20061213	CN 2004-80033115
20041028			
BR 2004015273	A	20061219	BR 2004-15273
20041028			
JP 2007510720	T	20070426	JP 2006-539492
20041028			
US 20070083046	A1	20070412	US 2006-577841
20060429			
US 7423037	B2	20080909	
MX 2006005226	A	20060720	MX 2006-5226
20060509			
KR 2006086408	A	20060731	KR 2006-708999
20060509			
KR 783855	B1	20071210	
NO 2006002700	A	20060808	NO 2006-2700
20060612			
PRIORITY APPLN. INFO.:			GB 2003-26148 A
20031110			
			US 2004-535459P P
20040109			
			WO 2004-US32771 W
20041028			
OTHER SOURCE(S):	CASREACT 142:482071; MARPAT 142:482071		
GI			



AB Title compds. I [X = OH, alkoxy, NH2, etc.; R independently = H, alkyl, with provisions; R1 = (un)substituted-alkyl, -alkoxy, CN, etc.; R2 = H, alkyl; R3 = H, alkyl; Ar = (un)substituted-Ph, -5- to 6-membered heteroaryl] and their pharmaceutically acceptable salts, are prepared and disclosed as norepinephrine reuptake inhibitors. Thus, e.g., II was prepared by conversion of 4-benzyl-morpholine-2-carbonitrile into the resp. carboxylic Et ester followed by amidation with N,N-dimethylhydroxylamine and subsequent Grignard reactions with Me magnesium bromide and 2-phenylbenzyl magnesium bromide followed by debenzylation and conversion into the HCl salt. The activity of I was evaluated in a CYP2D6 inhibition assay and preferred compds. of the invention exhibited an IC50 higher than 6 µM. I as norepinephrine reuptake inhibitors should prove useful in the treatment of disorders that are associated with norepinephrine dysfunction. Pharmaceutical compns. comprising I are disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

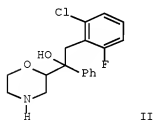
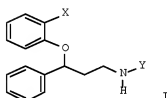
RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L21 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STM
 ACCESSION NUMBER: 2005:216719 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291416
 TITLE: Treatment of stuttering and other communication disorders with norepinephrine reuptake inhibitors
 INVENTOR(S): Kelsey, Douglas Kenneth
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 299 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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20040825	WO 2005021095	A2	20050310	WO 2004-US25591	
	WO 2005021095	A3	20050609		
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NA, NI,	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
SL, SY,	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				
ZM, ZW	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,				

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 RO, SE,
 MR, NE,
 SN, TD, TG
 CA 2532349 A1 20050310 CA 2004-2532349
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 EP 1660185 A2 20060531 EP 2004-780429
 20040825
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 US 20070032554 A1 20070208 US 2006-568269
 20060214
 PRIORITY APPLN. INFO.: US 2003-498018P P
 20030827 WO 2004-US25591 W
 20040825
 OTHER SOURCE(S): MARPAT 142:291416
 GI



AB Provided are methods and medicaments for treating stuttering or another communication disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The

invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone with 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation. The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

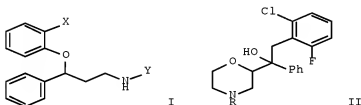
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:216660 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291415
 TITLE: Treatment of pervasive development disorders employing norepinephrine reuptake inhibitors
 INVENTOR(S): Allen, Albert John; Kelsey, Douglas Kenneth
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 300 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005020976	A2	20050310	WO 2004-US25593	
20040825				
WO 2005020976	A3	20050616		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2536161	A1	20050310	CA 2004-2536161	

20040825
 EP 1660065 A2 20060531 EP 2004-780431
 20040825 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
 US 20060241188 A1 20061026 US 2006-568466
 20060214
 PRIORITY APPLN. INFO.: US 2003-498146P P
 20030827 WO 2004-US25593 W
 20040825
 OTHER SOURCE(S): CASREACT 142:291415; MARPAT 142:291415
 GI



AB Provided are methods and medicaments for treating a pervasive development disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl (R = H) was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone by 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation of the obtained alc. I (R = Bn). The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

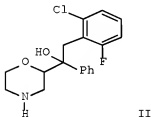
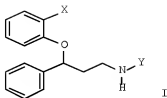
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:216659 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291414
 TITLE: Treatment of learning disabilities and motor skills
 disorder with norepinephrine reuptake

inhibitors
 INVENTOR(S): Sumner, Calvin Russell
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 304 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	WO 2005020975	A2	20050310	WO 2004-US25592	
20040825	WO 2005020975	A3	20050602		
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GB, GD,	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				
KZ, LC,	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
NA, NI,	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
SL, SY,	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				
ZM, ZW	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,				
ZW, AM,	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,				
DE, DK,	AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,				
RO, SE,	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,				
MR, NE,	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,				
	SN, TD, TG				
CA 2530014	A1	20050310	CA 2004-2530014		
20040825	EP 1660064	A2	20060531	EP 2004-780430	
20040825	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT,	IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 20070105960	A1	20070510	US 2006-568244	
20060214					
PRIORITY APPLN. INFO.:				US 2003-498019P	P
20030827				WO 2004-US25592	W
20040825					
OTHER SOURCE(S):	MARPAT 142:291414				
GI					



AB Provided are methods and medicaments for treating a learning disability or a motor skills disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone with 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation. The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

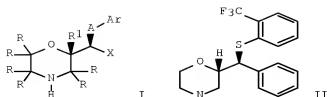
RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L21 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:182714 CAPLUS Full-text
 DOCUMENT NUMBER: 140:235724
 TITLE: Preparation of benzyl morpholine derivatives capable of selectively inhibiting norepinephrine reuptake
 INVENTOR(S): Walter, Magnus Wilhelm; Clark, Barry Peter; Gallagher, Peter Thaddeus; Haughton, Helen Louise; Rudyk, Helene
 Catherine Eugenie
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 81 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
20030818	A2	20040304	WO 2003-US23269	
WO 2004017977				
WO 2004017977	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2003269923	A1	20040311	AU 2003-269923	
20030818	A2	20050601	EP 2003-751812	
EP 1534291				
20030818	B1	20081112		
EP 1534291				
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AT 413882	T	20081115	AT 2003-751812	
20030818	A1	20060216	US 2005-524650	
US 20060035894				
20050217	B2	20080610		
US 7384941				
PRIORITY APPLN. INFO.:			GB 2002-19690	A
20020823			US 2002-415328P	P
20021001			WO 2003-US23269	W
20030818				
OTHER SOURCE(S):	MARPAT	140:235724		
GI				



AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl group, a cycloalkyl group or cycloalkylmethyl group] and pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared via substitution of (2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (preparation given) with 2-trifluoromethylthiophenol with subsequent debenzoylation. I have been found to exhibit a Ki value less than 500nM at the norepinephrine transporter as determined by scintillation proximity assays. In addition, I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

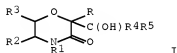
L21 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1999:232336 CAPLUS Full-text
 DOCUMENT NUMBER: 131:5228
 TITLE: A new synthesis of 2-(1-hydroxyalkyl)- and 2-(1-aminoalkyl)morpholines via 3-morpholinones
 AUTHOR(S): Dobrev, Alexander; Nechev, Lubomir; Ivanov, Christo; Bon, Maryse
 CORPORATE SOURCE: Faculty of Chemistry, University of Sofia, Sofia, 1126, Bulg.
 SOURCE: Journal of Chemical Research, Synopses (1999), (3), 188-189, 1001-1047
 CODEN: JRPSDC; ISSN: 0308-2342
 PUBLISHER: Royal Society of Chemistry
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 131:5228
 AB A new pathway for the synthesis of 2-(1-hydroxyalkyl)- and 2-[(aryl(amino)alkyl)morpholines via α -hydroxy- or α -aminoalkylation

of 3-morpholinones, followed by reduction with LiAlH₄ of the intermediate compds. to the target substituted morpholines, is described.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:534063 CAPLUS Full-text
DOCUMENT NUMBER: 111:134063
ORIGINAL REFERENCE NO.: 111:22443a,22446a
TITLE: Addition of the lithium derivatives of
4-alkyl-3-morpholinones to carbonyl compounds
AUTHOR(S): Dobrev, A.; Nechev, L.; Ivanov, Kh.
CORPORATE SOURCE: Fac. Chem., Univ. Sofia, Sofia, 1126, Bulg.
SOURCE: Liebigs Annalen der Chemie (1989), (8), 815-18
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:134063
GI

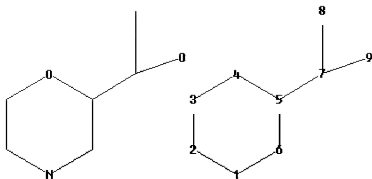


AB (Hydroxyalkyl)morpholinones I [R = H, Me, Ph; R1 = Me, Et, CHMe₂, Ph, CH₂Ph; R2 = H, Me; R3 = H, Me, Ph; R4 = Ph, p-anisyl, CCl₃, CMe₃; R5 = H, Me, Ph; R4R5 = (CH₂)₅] were prepared by reaction of 4-alkyl-3-morpholinones with carbonyl compds. in the presence of LDA. Many of the products were diastereomeric mixts.; for I (R = R2 = R3 = R5 = H, R1 = Me, R4 = p-anisyl), the erythro and threo isomers were separated. The conformation of the diastereoisomers was discussed.

<http://www.cas.org/support/stngen/stdoc/properties.html>

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7 8 9
ring nodes :
1 2 3 4 5 6
chain bonds :
5-7 7-8 7-9
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-9
exact bonds :
5-7 7-8

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS
9:CLASS

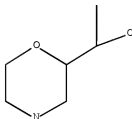
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L22 STRUCTURE UPLOADED

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L22 HAS NO ANSWERS

L22 STR



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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SAMPLE SCREEN SEARCH COMPLETED - 481 TO ITERATE

100.0% PROCESSED 481 ITERATIONS 27
ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8305 TO 10935
PROJECTED ANSWERS: 229 TO 851

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L25 20 L24

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L26 194 L23

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3972562 PRY<2003
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L28 2 L27 AND (?EPINEPHRINE?)

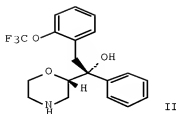
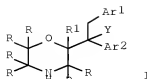
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L28 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:182855 CAPLUS Full-text
DOCUMENT NUMBER: 140:217649
TITLE: Preparation of aryl and heteroaryl morpholine
derivatives as norepinephrine reuptake
inhibitors
INVENTOR(S): Cases-Thomas, Manuel Javier; Houghton, Helen
Louise;
Lamas-Peteira, Carlos; Ouwerkerk-Mahadevan,
Sivi;

Rudyk, Masters, John Joseph; Simmonds, Robin George;
 Helene Catherine Eugenie; Walter, Magnus
 Wilhelm
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 82 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004018441	A1	20040304	WO 2003-US23270	
20030818 <--				
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20030818				
OTHER SOURCE(S):	MARPAT	140:217649		
GI				



AB Morpholine derivs. of formula I [R = independently H, alkyl; R1 = H, alkyl; Y = OH, alkoxy; Ar1, Ar2 = (substituted) Ph, (substituted) heteroaryl] are prepared. The compds. are selective inhibitors of the reuptake of norepinephrine. Thus, II.HCl was prepared from (4-benzylmorpholin-2-yl)-phenylmethanone (preparation given) and 2-(trifluoromethoxy)benzyl bromide. The compds. had Ki values less than 500 nM at the norepinephrine transporter in a scintillation proximity assay.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:182714 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:235724

TITLE: Preparation of benzyl morpholine derivatives capable

of selectively inhibiting norepinephrin

reuptake

INVENTOR(S):

Walter, Magnus Wilhelm; Clark, Barry Peter;

Gallagher,

Peter Thaddeus; Haughton, Helen Louise; Rudyk,

Helene

Catherine Eugenie

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE:

PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

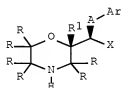
English

FAMILY ACC. NUM. COUNT: 1

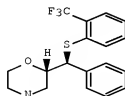
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 TM, TN, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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 US 20060035894 A1 20060216 US 2005-524650
 20050217 <--
 US 7384941 B2 20080610
 PRIORITY APPLN. INFO.: GB 2002-19690 A
 20020823 <-- US 2002-415328P P
 20021001 <-- WO 2003-US23269 W
 20030818
 OTHER SOURCE(S): MARPAT 140:235724
 GI



I



II

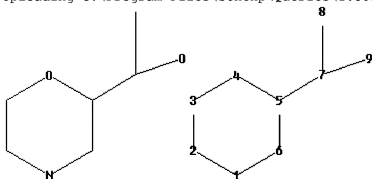
AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl

group, a cycloalkyl group or cycloalkylmethyl group] and pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared via substitution of (2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (preparation given) with 2-trifluoromethylthiophenol with subsequent debenzoylation. I have been found to exhibit a K_i value less than 500nM at the norepinephrine transporter as determined by scintillation proximity assays. In addition, I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.

<http://www.cas.org/support/stngen/stndoc/properties.html>

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7 8 9

ring nodes :

1 2 3 4 5 6

chain bonds :

5-7 7-8 7-9

ring bonds :

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exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-9

exact bonds :

5-7 7-8

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS

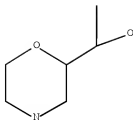
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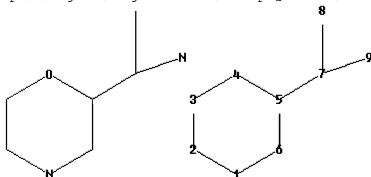
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Structure attributes must be viewed using STN Express query preparation.

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ring nodes :

1 2 3 4 5 6

chain bonds :

5-7 7-8 7-9

ring bonds :

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exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-9

exact bonds :

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Match level :

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9:CLASS

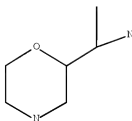
L31 STRUCTURE UPLOADED

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L31 HAS NO ANSWERS

L31

STR



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

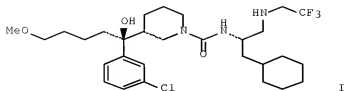
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L34 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:365001 CAPLUS Full-text
 DOCUMENT NUMBER: 144:432692
 TITLE: Preparation of diaminoalkanes, particularly
 N-(1-aminopropan-2-yl)piperidine-1-
 carboxamides, as
 aspartic protease inhibitors
 INVENTOR(S): Baldwin, John J.; Claremon, David A.; Tice,
 Colin;
 Cacatian, Salvation; Dillard, Lawrence W.;
 Ishchenko,
 Alexey V.; Yuan, Jing; Xu, Zhenrong; McGeehan,
 Gerard;
 Zhao, Wei; Simpson, Robert D.; Singh, Suresh
 B.;
 Flaherty, Patrick T.; Wery, Jean-Pierre
 PATENT ASSIGNEE(S): Vitae Pharmaceutical, Inc, USA
 SOURCE: PCT Int. Appl., 755 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

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		GB, GD,		

KR, KZ, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP,
 MX, MZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW,
 SE, SG, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
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 YU, ZA, ZM, ZW
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 AZ, BY, KG, KZ, MD, RU, TJ, TM
 AU 2005294123 A1 20060420 AU 2005-294123
 20051007 CA 2582202 A1 20060420 CA 2005-2582202
 20051007 EP 1807078 A1 20070718 EP 2005-807547
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 CN 101072561 A 20071114 CN 2005-80042064
 20051007 BR 2005016132 A 20071204 BR 2005-16132
 20051007 JP 2008515916 T 20080515 JP 2007-535853
 20051007 MX 200703858 A 20071211 MX 2007-3858
 20070329 KR 2007084040 A 20070824 KR 2007-710366
 20070507 IN 2007CN01935 A 20070831 IN 2007-CN1935
 20070507 US 20090018103 A1 20090115 US 2008-664558
 20080123
 PRIORITY APPLN. INFO.: US 2004-616770P P
 20041007 WO 2005-US36230 W
 20051007
 OTHER SOURCE(S): CASREACT 144:432692; MARPAT 144:432692
 GI



AB The invention is related to diaminoalkanes of formula R1-X-(CR2R3)-Y-A-Q-N(R4)-L-G (I; R1 = halocyclo/cyclo/alkyl, (un)substituted Ph, naphthyl, heteroaryl, etc.; X, Y = independently CH2 or a single bond; R2 = (un)substituted alk(en/yn)yl, alkoxyalkyl, aminocarbonylaminoalkyl, aminosulfonylaminoalkyl, etc.; R3 = H, alkyl, OH and derivs., alkylaminosulfonylamino, (un)substituted phenylamino, heteroarylamino; A = (un)saturated (un)substituted 4- to 7-membered ring, which is optionally bridged by (CH2)m via bonds to 2 members of said ring; Q and Y are attached to C or N atoms in ring A in a 1,2 or 1,3 or 1,4 relationship; Q = divalent radical selected from CO, C:S, SO2, CO-CO, CO-CH2-CO, etc.; m = 1-3; R4 = H, halo/alkoxy/cyano/alkyl; L = (un)substituted linear (C2-C4)alkyl chain when G = OH, OR9, NH2, NHR9, NR9R10, NHC(:NH)NH2, or NHC(:NH)NHR9; or L = (un)substituted linear (C1-C3)alkyl chain when G = C(:NH)NH2, or C(:NH)NHR9; G = OH, OR9, NH2, NHR9, NR9R10, NHC(:NH)NH2, NHC(:NH)NHR9, C(:NH)NH2, C(:NH)NHR9; R9 = halo/alkyl, (un)substituted Ph, naphthyl, heteroaryl, heteroarylsulfinyl, naphthyl, etc.; R10 = halo/alkyl; with provisos;), and their enantiomers, diastereomers, and salts, e.g. II, which are orally active and bind to aspartic proteases to inhibit their activity. I are useful in the treatment or amelioration of diseases associated with elevated levels of aspartic protease activity. Thus, reacting benzyl N-((S)-2-amino-3-cyclohexylpropyl)-N-(2,2,2-trifluoroethyl)carbamate (preparation given) with ((S)-1-(3-chlorophenyl)-5-methoxy-1-((3R)-piperidin-3-yl)pentan-1-ol and CDI in the presence of DIEA in CH2Cl2, followed by Cbz-deprotection gave piperidine II. Selected I had an IC50 in the range of 0.001 nM to 5 nM for the inhibition of renin activity. I are useful in ameliorating or treating aspartic protease related disorders, such as hypertension, congestive heart failure, cardiac hypertrophy, cardiac fibrosis, etc. cardiomyopathy postinfarction, nephropathy, vasculopathy and neuropathy, diseases of the coronary vessels.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE

L34 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:451370 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:482071

TITLE: Preparation of morpholine derivatives as norepinephrine reuptake inhibitors

INVENTOR(S): Campbell, Gordon Iain; Cases-Thomas, Manuel Javier;

Helene

Man, Teresa; Masters, John Joseph; Rudyk,

PATENT ASSIGNEE(S):

Catherine Eugenie; Walter, Magnus Wilhelm

SOURCE:

Eli Lilly and Company, USA

PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

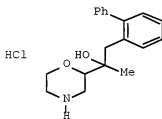
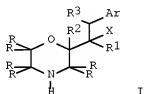
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PATENT INFORMATION:

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EP 1682523	A1	20060726	EP 2004-794209	
20041028				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,				
PL, SK, HR				
CN 1878762	A	20061213	CN 2004-80033115	
20041028				
BR 2004015273	A	20061219	BR 2004-15273	
20041028				
JP 2007510720	T	20070426	JP 2006-539492	
20041028				
US 20070083046	A1	20070412	US 2006-577841	
20060429				
US 7423037	B2	20080909		
MX 2006005226	A	20060720	MX 2006-5226	

20060509	KR 2006086408	A	20060731	KR 2006-708999	
20060509	KR 783855	B1	20071210		
	NO 2006002700	A	20060808	NO 2006-2700	
20060612					
PRIORITY APPLN. INFO.:				GB 2003-26148	A
20031110				US 2004-535459P	P
20040109				WO 2004-US32771	W
20041028					
OTHER SOURCE(S):	CASREACT 142:482071; MARPAT 142:482071				
GI					



AB Title compds. I [X = OH, alkoxy, NH₂, etc.; R independently = H, alkyl, with provisions; R₁ = (un)substituted-alkyl, -alkoxy, CN, etc.; R₂ = H, alkyl; R₃ = H, alkyl; Ar = (un)substituted-Ph, -5- to 6-membered heteroaryl] and their pharmaceutically acceptable salts, are prepared and disclosed as norepinephrine reuptake inhibitors. Thus, e.g., II was prepared by conversion of 4-benzyl-morpholine-2-carbonitrile into the resp. carboxylic Et ester followed by amidation with N,N-dimethylhydroxylamine and subsequent Grignard reactions with Me magnesium bromide and 2-phenylbenzyl magnesium bromide followed by debenzylation and conversion into the HCl salt. The activity of I was evaluated in a CYP2D6 inhibition assay and preferred compds. of the invention exhibited an IC₅₀ higher than 6 μM. I as norepinephrine reuptake inhibitors should prove useful in the treatment of disorders that are associated with norepinephrine dysfunction. Pharmaceutical compns. comprising I are disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L34 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:12274 CAPLUS Full-text
DOCUMENT NUMBER: 134:86272
TITLE: Preparation of pyrimidine derivatives as Src-
family
protein tyrosine kinase inhibitor compounds
INVENTOR(S): Hunt, Julianne A.; Mills, Sander G.; Sinclair,
Peter
J.; Zaller, Dennis M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	----

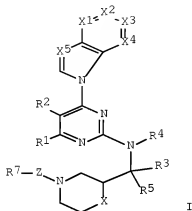
WO 2001000214	A1	20010104	WO 2000-US17472	
20000626				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,				
CH, CN,				
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH,				
GM, HR,				
HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,				
LT, LU,				
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,				
RU, SD,				
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,				
VN, YU,				
ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,				
CH, CY,				
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,				
BF, BJ,				
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2376951	A1	20010104	CA 2000-2376951	
20000626				
US 6316444	B1	20011113	US 2000-603699	
20000626				
EP 1194152	A1	20020410	EP 2000-944858	
20000626				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT,				
IE, SI, LT, LV, FI, RO				
JP 2003503354	T	20030128	JP 2001-505923	
20000626				
PRIORITY APPLN. INFO.:			US 1999-141597P	P
19990630			WO 2000-US17472	W

20000626

OTHER SOURCE(S):

MARPAT 134:86272

GI



I

AB What are claimed are pyrimidine compds. (shown as I), or their pharmaceutically acceptable salts, hydrates, solvates, crystal forms and individual diastereomers, and pharmaceutical compns. including the same and their use as inhibitors of tyrosine kinase enzymes and consequently their use in the prophylaxis and treatment of protein tyrosine kinase-associated disorders, such as immune diseases, hyperproliferative disorders and other diseases in which inappropriate protein kinase action is believed to play a role, such as cancer, angiogenesis, atherosclerosis, graft rejection, rheumatoid arthritis and psoriasis. In I, R1, R2 = independently H, halo, OH, SH, CN, NO2, alkyl, alkoxy, acyloxy, alkoxycarbonyloxy, carbamoyloxy, alkylthio, sulfinyl, sulfonyl, acyl, alkoxycarbonyl, carbamoyl, amino, acylamino, alkoxycarbonylamino, ureido, sulfamoyl, sulfonylamino, or R1 and R2 can join together to form a fused methylenedioxy ring or a fused 6-membered aromatic ring; terms such as 'alkyl' here and below are further defined in the claims. R3, R5 = independently H, C1-C6-alkyl unsubstituted or substituted with 1-3 substituents, aryl (Ph or naphthyl unsubstituted or substituted with 1-3 substituents), or R3 and R5 taken together can represent :O. R4 = H, C1-C6-alkyl, C1-C6-alkoxyl, or R4 and X can join together to form a 5- or 6-membered ring with substituted methylene or ethylene. X1, X2, X3, X4 in -X1:X2-X3:X4- are substituted CH or N where 0-2 of X1, X2, X3, X4 are N. X5 = N, CH. R7 = H, alkyl, alkoxy, amino. X = O, S, SO, SO2, imino. Z = C=O, SO2, substituted P(=O)(OH) or a single bond. 44 Example prepn. are given, but no preparative method is claimed and no data relating to the usefulness of the compds. are given.

REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE

FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

=> s l32 and (central nervous system or CNS)

194 L32
454841 CENTRAL
40 CENTRALS
454870 CENTRAL
(CENTRAL OR CENTRALS)
241203 NERVOUS
2736397 SYSTEM
1472370 SYSTEMS
3691088 SYSTEM
(SYSTEM OR SYSTEMS)
91474 CENTRAL NERVOUS SYSTEM
(CENTRAL(W)NERVOUS(W)SYSTEM)
44165 CNS

L35 3 L32 AND (CENTRAL NERVOUS SYSTEM OR CNS)

=> d l35 ibib abs 1-3

L35 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:605280 CAPLUS Full-text

DOCUMENT NUMBER: 145:83221

TITLE: Preparation of bridged arylpiperidines as nkl
antagonists

INVENTOR(S): Xiao, Dong; Palani, Anandan; Wang, Cheng;

Tsui,

Hon-Chung; Huang, Xianhai; Shah, Sapna S.;

Rao, Ashwin

U.; Chen, Xiao; Paliwal, Sunil; Shih, Neng-

Yang

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 202 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	----
WO 2006065654	A1	20060622	WO 2005-US44647	
20051207				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,			
CA, CH,	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,			
GB, GD,	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,			
KP, KR,	KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,			
MW, MX,	MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,			
SD, SE,	SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,			
UZ, VC,				

VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,
 BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,
 BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 US 20060258665 A1 20061116 US 2005-291363
 20051201
 US 7354922 B2 20080408
 CA 2591079 A1 20060622 CA 2005-2591079
 20051207
 EP 1828188 A1 20070905 EP 2005-849677
 20051207
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK,
 TR, AL,
 BA, HR, MK, YU
 JP 2008523144 T 20080703 JP 2007-546775
 20051207
 MX 200707152 A 20070814 MX 2007-7152
 20070614
 CN 101115753 A 20080130 CN 2005-80048054
 20070813
 PRIORITY APPLN. INFO.: US 2004-635971P P
 20041214
 WO 2005-US44647 W
 20051207
 OTHER SOURCE(S): MARPAT 145:83221
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. I [Arl-2 independently = (un)substituted aryl or heteroaryl; X1 = O, NH, N-alkyl, N-haloalkyl, etc.; X2 = O, CH2, C(alkyl)2, NH, N-alkyl, etc.; X3 = CO, CH2, C(alkyl)2, C(=N-alkyl), etc.; X4 = NH, N-alkyl, CH2, etc.; with provision that when X3 = (un)substituted C, at least one of X2 and X4 also equal (un)substituted C; n = 0-4; R1 = H, OH, (un)substituted alkyl, etc.; R2-5 independently = H, haloalkyl, cycloalkyl, etc.; further provisions allow for when X2 = N the substituent on N may together with R1 form a (un)substituted ring], and their pharmaceutically acceptable salts, were prepared and disclosed as useful in treating diseases or conditions mediated by NK1 receptors, for example various physiol. disorders, symptoms or diseases, including emesis, depression, anxiety and cough. Thus, e.g., II was prepared in a multistep synthesis from III. Especially preferred compds. of the invention have Ki values of 0.05 nM to about 1 nM for the NK1 receptor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L35 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1176480 CAPLUS Full-text
DOCUMENT NUMBER: 143:440426
TITLE: Substituted morpholine compounds for the
treatment of

central nervous system
disorders, their preparation and
pharmaceutical

compositions
INVENTOR(S): Barta, Nancy S.; Glase, Shelly Ann; Gray,
David L.; Reichard, Gregory A.; Simons, Lloyd J.; Xu,
Weijan

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 85 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050245519	A1	20051103	US 2005-119210	
20050429				
AU 2005238296	A1	20051110	AU 2005-238296	
20050419				
CA 2564994	A1	20051110	CA 2005-2564994	
20050419				
WO 2005105763	A1	20051110	WO 2005-1B1158	
20050419				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,				
CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				
GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP,				
KR, KZ,				
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,				
MZ, NA,				
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,				
SK, SL,				
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,				
YU, ZA,				
ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,				
ZW, AM,				
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,				
DE, DK,				
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL,				
PL, PT,				
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,				

GW, ML, MR, NE, SN, TD, TG
 EP 1745029 A1 20070124 EP 2005-733459
 20050419
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR,
 AL, BA, HR, LV, MK, YU
 CN 1950348 A 20070418 CN 2005-80013776
 20050419
 BR 2005010453 A 20071030 BR 2005-10453
 20050419
 JP 2007535530 T 20071206 JP 2007-510153
 20050419
 JP 4185154 B2 20081126
 NL 1028924 A1 20051101 NL 2005-1028924
 20050429
 NL 1028924 C2 20060427
 IN 2006DN05782 A 20070803 IN 2006-DN5782
 20061005
 MX 2006012505 A 20061215 MX 2006-12505
 20061027
 KR 2007006881 A 20070111 KR 2006-722767
 20061030
 NO 2006005456 A 20070104 NO 2006-5456
 20061127
 JP 2008019267 A 20080131 JP 2007-233201
 20070907
 PRIORITY APPLN. INFO.: US 2004-567244P P
 20040430
 JP 2007-510153 A3
 20050419
 WO 2005-IB1158 W
 20050419
 OTHER SOURCE(S): CASREACT 143:440426; MARPAT 143:440426
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB The invention relates to compds. of the formula I, which can be
 used in the treatment of central nervous system disorders. In
 compds. I, A is O or S; X is C1-10 alkyl, C2-8 alkenyl, aryl,
 heterocyclyl, C1-6 alkoxy, etc., with each group optionally
 substituted; and R1 - R5 are independently selected from H, OH,
 halo, C1-6 alkyl, aryl, C3-8 cycloalkyl, C2-6 alkenyl, C1-6
 alkoxy, aryloxy, heterocyclyl, etc.; including pharmaceutically
 acceptable salts, enantiomers and diastereomers. The invention
 also relates to the preparation of I, pharmaceutical compns.
 comprising a compound I and a pharmaceutically acceptable carrier,
 as well as to the use of the compns. in the treatment of central
 nervous system disorders. Ring opening of (R,R)-phenylglycidol
 with 1-naphthol followed by silylation of the primary alc.,

mesylation of the secondary alc., and desilylation gave mesylate II, which underwent ring closure to the epoxide, ring opening with ammonium hydroxide and amidation with chloroacetyl chloride, resulting in the formation of amide III. Compound III was converted to the morpholine by intramol. cyclization and Red-Al reduction to give morpholine IV. Several compds., e.g., IV, express high inhibition of human norepinephrine transporter (hNET) and human serotonin transporter (hSERT).

L35 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1971:476811 CAPLUS Full-text

DOCUMENT NUMBER: 75:76811

ORIGINAL REFERENCE NO.: 75:12167a,12170a

TITLE: Pharmacologically active morpholine

derivatives

INVENTOR(S): McLoughlin, Bernard J.

PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd.

SOURCE: Ger. Offen., 51 pp. Addn. to Ger. Offen.

1,695,295.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
----	---	----	-----	----
DE 2056589	A	19710527	DE 1970-2056589	
19701117				
GB 1295447	A	19721108	GB 1969-56086	
19691117				
ZA 7007662	A	19710825	ZA 1970-7662	
19701112				
NL 7016833	A	19710519	NL 1970-16833	
19701117				
FR 2073375	A6	19711001	FR 1970-41208	
19701117				
FR 2073375	B2	19741011		
AT 302341	B	19721010	AT 1970-10362	
19701117				
CH 531528	A	19730131	CH 1970-17076	
19701117				
SU 373945	A3	19730312	SU 1970-1494684	
19701117				
AT 306045	B	19730326	AT 1971-8261	
19701117				
ES 385627	A2	19730501	ES 1970-385627	
19701117				
CH 540277	A	19730928	CH 1972-1525	
19701117				
CH 540278	A	19730928	CH 1972-1526	
19701117				
SU 422159	A3	19740330	SU 1970-1716174	
19701117				
IL 35738	A	19740630	IL 1970-35738	

19701127

PRIORITY APPLN. INFO.:

GB 1969-56086

A

19691117

GI For diagram(s), see printed CA Issue.

AB Morpholine derivs. (I, Y = H₂) with sedative activity on the central nervous system are prepared. Thus, to a solution of trimethylsulfoxonium iodide in Me₂SO, 50% oily NaH suspension was added in a N atmospheric at 50-60° to give a mixture containing dimethylsulfonyl methylide. A solution of phenoxyacetone in Me₂SO was added and the mixture heated 3 hr at 50-60° to give 1,2-epoxy-2-methyl-3-phenoxypropane (II). Heating II with PhCH₂NH₂ at 140° gave PhOCH₂CMe(OH)CH₂NHCH₂Ph III. Reaction of III in CH₂Cl₂ with ClCH₂COCl and NEt₃ at <10° gave 1-(N-benzylchloroacetamido)-2-methyl-3-phenoxy-2-propanol, cyclized with methanolic MeONa to I (Y = O, R₁ = CH₂Ph, R₂ = Me, R₃ = R₄ = H, X = Ph) (IV). Reduction of IV in Et₂O with LiAlH₄ gave I (Y = H₂, R₁ = CH₂Ph, R₂ = Me, R₃ = R₄ = H, X = Ph), isolated as the HCl salt, and debenzylated by hydrogenation with Pd/C to I (Y = H₂, R₁ = R₄ = R₃ = H, R₂ = Me, X = Ph). By similar methods, an addnl. 25 I were prepared

=> s 132 and (serotonin or ?epinephrin? or adrenerg? or dopamin?)

194 L32

76807 SEROTONIN

53 SEROTONINS

76812 SEROTONIN

(SEROTONIN OR SEROTONINS)

66707 ?EPINEPHRIN?

78657 ADRENERG?

107711 DOPAMIN?

L36

15 L32 AND (SEROTONIN OR ?EPINEPHRIN? OR ADRENERG? OR DOPAMIN?)

=> s 136 ibib abs 1-15

MISSING OPERATOR L36 IBIB

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s 136 ibib abs 1-15

MISSING OPERATOR L36 IBIB

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> d 136 ibib abs 1-15

L36 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:

2008:1249137 CAPLUS Full-text

DOCUMENT NUMBER:

150:20056

TITLE:

Design and synthesis of reboxetine analogs

morpholine

derivatives as selective nor^oepinephrine
reuptake inhibitors

AUTHOR(S):

Xu, Wenjian; Gray, David L.; Glase, Shelly A.;

Barta,

Nancy S.

CORPORATE SOURCE: Department of Chemistry, Pfizer Global
 Research & Development Groton Laboratories, Ann Arbor,
 MI, 48105, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters
 (2008), 18(20), 5550-5553
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB As part of a discovery effort aimed at identifying novel
 norepinephrine reuptake inhibitors (NRIs), a number of substituted
 morpholines were designed and synthesized. The target compds.
 contain vicinal stereogenic centers, and the program was greatly
 facilitated by the adoption of efficient synthetic routes which
 allowed for the late stage incorporation of structural and
 physicochem. diversity into the targets. Structure-activity
 relationships were developed by optimizing individual ring
 components of the structure for NRI potency and for selectivity
 against other monoamine reuptake transporters. Several novel
 morpholine derivs. with a potent and selective NRI profile are
 described.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L36 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2008:95116 CAPLUS Full-text
 DOCUMENT NUMBER: 148:160156
 TITLE: Biomarker-optimized attention deficit-
 hyperactivity disorder (ADHD) treatment with selective
 norepinephrine reuptake inhibitors
 INVENTOR(S): Lawrence, Donald Gilbert
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 8pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080020387	A1	20080124	US 2007-694099	
20070330				
PRIORITY APPLN. INFO.:			US 2006-788008P	P
20060331				
AB	The invention provides methods for predicting patient responsiveness to treatment of attention-deficit/hyperactivity disorder (ADHD) with selective norepinephrine reuptake inhibitors; identifying individuals requiring a higher than normal dose of atomoxetine for treating ADHD; and predicting patient			

responsiveness to treatment of neuropsychiatric diseases or disorders responsive to treatment with selective norepinephrine reuptake inhibitors are provided. These methods are based on the identification of the variable number of tandem repeats (VNTR) polymorphism present in the 3'-untranslated region of the human dopamine transporter 1 (DAT 1) gene present in patient body fluid or tissue samples. Patients with a 10/10 VNTR genotype are considered poor responders to treatment with atomoxetine and other selective norepinephrine reuptake inhibitors for the indicated conditions.

L36 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2006:1331209 CAPLUS Full-text
 DOCUMENT NUMBER: 146:223523
 TITLE: Synthesis of ¹¹C-labelled (R)-OHDMI and CFMME
 and their evaluation as candidate radioligands for
 imaging central norepinephrine transporters with PET
 AUTHOR(S): Schou, Magnus; Pike, Victor W.; Sovago, Judit;
 Gulyas, Balazs; Gallagher, Peter T.; Dobson, David R.;
 Walter, Magnus W.; Rudyk, Helene; Farde, Lars;
 Halldin, Christer
 CORPORATE SOURCE: Karolinska Institutet, Department of Clinical
 Neuroscience, Psychiatry Section, Karolinska
 Hospital, Stockholm, S-17176, Swed.
 SOURCE: Bioorganic & Medicinal Chemistry (2007),
 15(2), 616-625
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 146:223523
 AB (R)-1-(10,11-Dihydro-dibenzo[b,f]azepin-5-yl)-3-methylamino-
 propan-2-ol ((R)-OHDMI) and (S,S)-1-cyclopentyl-2-(5-fluoro-2-
 methoxy-phenyl)-1- morpholin-2-yl-ethanol (CFMME) were synthesized
 and found to be potent inhibitors of norepinephrine reuptake.
 Each was labeled efficiently in its Me group with carbon-11 (t_{1/2}
 = 20.4 min) as a prospective radioligand for imaging brain
 norepinephrine transporters (NET) with positron emission tomog.
 (PET). The uptake and distribution of radioactivity in brain
 following i.v. injection of each radioligand into cynomolgus
 monkey was examined in vivo with PET. After injection of (R)-
 [¹¹C]OHDMI, the maximal whole brain uptake of radioactivity was
 very low (1.1% of injected dose; I.D.). For occipital cortex,
 thalamus, lower brainstem, mesencephalon and cerebellum,
 radioactivity ratios to striatum at 93 min after radioligand
 injection were 1.35, 1.35, 1.2, 1.2 and 1.0, resp. After
 injection of [¹¹C]CFMME, radioactivity readily entered brain (3.5%
 I.D.). Ratios of radioactivity to cerebellum at 93 min for
 thalamus, occipital cortex, region of locus coeruleus,

mesencephalon and striatum were 1.35, 1.3, 1.3, 1.2 and 1.2, resp. Radioactive metabolites in plasma were measured by radio-HPLC. (R)-[11C]OHDMI represented 75% of plasma radioactivity at 4 min after injection and 6% at 30 min. After injection of [11C]CFMME, 84% of the radioactivity in plasma represented parent at 4 min and 20% at 30 min. Since the two new hydroxylated radioligands provide only modest regional differentiation in brain uptake and form potentially troublesome lipophilic radioactive metabolites, they are concluded to be inferior to existing radioligands, such as (S,S)-[11C]MeNER, (S,S)-[18F]MeNER-D2 and (S,S)-[18F]FRB-D4, for the study of brain NETs with PET in vivo.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L36 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:605280 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 145:83221

TITLE: Preparation of bridged arylpiperidines as nk1 antagonists

INVENTOR(S): Xiao, Dong; Palani, Anandan; Wang, Cheng; Tsui,

Hon-Chung; Huang, Xianhai; Shah, Sapna S.;

Rao, Ashwin

U.; Chen, Xiao; Paliwal, Sunil; Shih, Neng-

Yang

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 202 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006065654	A1	20060622	WO 2005-US44647	
20051207				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,			

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,
 BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 US 20060258665 A1 20061116 US 2005-291363
 20051201 US 7354922 B2 20080408
 CA 2591079 A1 20060622 CA 2005-2591079
 20051207 EP 1828188 A1 20070905 EP 2005-849677
 20051207 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK,
 TR, AL, BA, HR, MK, YU
 JP 2008523144 T 20080703 JP 2007-546775
 20051207 MX 200707152 A 20070814 MX 2007-7152
 20070614 CN 101115753 A 20080130 CN 2005-80048054
 20070813 PRIORITY APPLN. INFO.: US 2004-635971P P
 20041214 WO 2005-US44647 W
 20051207
 OTHER SOURCE(S): MARPAT 145:83221
 GI

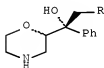
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. I [Arl-2 independently = (un)substituted aryl or heteroaryl; X1 = O, NH, N-alkyl, N-haloalkyl, etc.; X2 = O, CH2, C(alkyl)2, NH, N-alkyl, etc.; X3 = CO, CH2, C(alkyl)2, C(=N-alkyl), etc.; X4 = NH, N-alkyl, CH2, etc.; with provision that when X3 = (un)substituted C, at least one of X2 and X4 also equal (un)substituted C; n = 0-4; R1 = H, OH, (un)substituted alkyl, etc.; R2-5 independently = H, haloalkyl, cycloalkyl, etc.; further provisions allow for when X2 = N the substituent on N may together with R1 form a (un)substituted ring], and their pharmaceutically acceptable salts, were prepared and disclosed as useful in treating diseases or conditions mediated by NK1 receptors, for example various physiol. disorders, symptoms or diseases, including emesis, depression, anxiety and cough. Thus, e.g., II was prepared in a multistep synthesis from III. Especially preferred compds. of the invention have Ki values of 0.05 nM to about 1 nM for the NK1 receptor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L36 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:188918 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 144:432755
 TITLE: Discovery of novel and selective tertiary
 alcohol containing inhibitors of the norepinephrine
 transporter
 AUTHOR(S): Cases-Thomas, Manuel J.; Masters, John J.;
 Walter, Magnus W.; Campbell, Gordon; Haughton, Louise;
 Gallagher, Peter T.; Dobson, David R.;
 Mancuso, Vincent; Bonnier, Benjamin; Giard, Thierry;
 Defrance, Thierry; Vanmarsenille, Michel; Ledgard,
 Andrew; White, Craig; Ouwerkerk-Mahadevan, Sivi;
 Brunelle, Francoise J.; Dezutter, Nancy A.; Herbots,
 Camy A.; Lienard, Joel Y.; Findlay, Jeremy; Hayhurst,
 Lorna; Boot, John; Thompson, Linda K.; Hemrick-
 Luecke, Susan
 CORPORATE SOURCE: Lilly Research Centre, Eli Lilly and Company,
 Ltd,
 Surrey, GU20 6PH, UK
 SOURCE: Bioorganic & Medicinal Chemistry Letters
 (2006), 16(7), 2022-2025
 CODEN: BMCLEB; ISSN: 0960-894X
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 144:432755
 GI



I



II

AB Nonracemic α -phenyl- α -(arylmethyl)-2-morpholinemethanol
 hydrochlorides **I**•HCl (R = Ph, 2-MeOC₆H₄, 3-MeOC₆H₄, 4-MeOC₆H₄, 2-
 ClC₆H₄, 2-BrC₆H₄, 2-EtOC₆H₄, 2-Me2CHOC₆H₄, 2-F3CSC₆H₄, 2-PhC₆H₄)
 are prepared as potent and selective inhibitors of the
 norepinephrine transporter. **I**•HCl (R = Ph, 2-MeOC₆H₄, 3-MeOC₆H₄,
 4-MeOC₆H₄, 2-ClC₆H₄, 2-BrC₆H₄, 2-EtOC₆H₄, 2-Me2CHOC₆H₄, 2-

F3CSC6H4, 2-PhC6H4) are prepared using the diastereoselective addition of arylmethyl Grignard reagents to nonracemic morpholinylphenylmethanone II as the key step; debenzoylation with 1-chloroethyl chloroformate and methanolysis provides the title compds. II is prepared in four steps by addition of 2-(benzylamino)ethanol to α -chloroacrylonitrile, cyclocondensation to the morpholinecarbonitrile, addition of phenylmagnesium chloride and hydrolysis to racemic II, and resolution of racemic II either by preparative HPLC or by preparative SFC. The in vitro binding affinities of I•HCl (R = Ph, 2-MeOC6H4, 3-MeOC6H4, 4-MeOC6H4, 2-ClC6H4, 2-BrC6H4, 2-ETOC6H4, 2-Me2CHOC6H4, 2-F3CSC6H4, 2-PhC6H4) and of the three diastereomers of I•HCl (R = 2-MeOC6H4) for the norepinephrine, dopamine and serotonin transporters are given; the in vivo activity of I•HCl (R = 2-MeOC6H4) in a pharmacodynamic animal model for norepinephrine reuptake inhibition is also given. The structure of I•HCl (R = 2-BrC6H4) is determined by X-ray crystallog.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1176480 CAPLUS Full-text

DOCUMENT NUMBER: 143:440426

TITLE: Substituted morpholine compounds for the treatment of

central nervous system disorders, their

and pharmaceutical compositions

INVENTOR(S): Barta, Nancy S.; Glase, Shelly Ann; Gray, David L.;

Reichard, Gregory A.; Simons, Lloyd J.; Xu,

WeiJan

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

SOURCE: U.S. Pat. Appl. Publ., 85 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050245519	A1	20051103	US 2005-119210	
20050429				
AU 2005238296	A1	20051110	AU 2005-238296	
20050419				
CA 2564994	A1	20051110	CA 2005-2564994	
20050419				
WO 2005105763	A1	20051110	WO 2005-1B1158	
20050419				
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CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				

GB, GD,
 KR, KZ,
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 SK, SL,
 YU, ZA,
 ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM,
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 PL, PT,
 GW, ML,
 MR, NE, SN, TD, TG
 EP 1745029 A1 20070124 EP 2005-733459
 20050419
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
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 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR,
 AL, BA,
 HR, LV, MK, YU
 CN 1950348 A 20070418 CN 2005-80013776
 20050419
 BR 2005010453 A 20071030 BR 2005-10453
 20050419
 JP 2007535530 T 20071206 JP 2007-510153
 20050419
 JP 4185154 B2 20081126
 NL 1028924 A1 20051101 NL 2005-1028924
 20050429
 NL 1028924 C2 20060427
 IN 2006DN05782 A 20070803 IN 2006-DN5782
 20061005
 MX 2006012505 A 20061215 MX 2006-12505
 20061027
 KR 2007006881 A 20070111 KR 2006-722767
 20061030
 NO 2006005456 A 20070104 NO 2006-5456
 20061127
 JP 2008019267 A 20080131 JP 2007-233201
 20070907
 PRIORITY APPLN. INFO.: US 2004-567244P P
 20040430
 JP 2007-510153 A3
 WO 2005-IB1158 W
 20050419
 20050419
 OTHER SOURCE(S): CASREACT 143:440426; MARPAT 143:440426
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB The invention relates to compds. of the formula I, which can be used in the treatment of central nervous system disorders. In compds. I, A is O or S; X is C1-10 alkyl, C2-8 alkenyl, aryl, heterocyclyl, C1-6 alkoxy, etc., with each group optionally substituted; and R1 - R5 are independently selected from H, OH, halo, C1-6 alkyl, aryl, C3-8 cycloalkyl, C2-6 alkenyl, C1-6 alkoxy, aryloxy, heterocyclyl, etc.; including pharmaceutically acceptable salts, enantiomers and diastereomers. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of central nervous system disorders. Ring opening of (R,R)-phenylglycidol with 1-naphthol followed by silylation of the primary alc., mesylation of the secondary alc., and desilylation gave mesylate II, which underwent ring closure to the epoxide, ring opening with ammonium hydroxide and amidation with chloroacetyl chloride, resulting in the formation of amide III. Compound III was converted to the morpholine by intramol. cyclization and Red-Al reduction to give morpholine IV. Several compds., e.g., IV, express high inhibition of human norepinephrine transporter (hNET) and human serotonin transporter (hSERT).

L36 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:588645 CAPLUS Full-text

DOCUMENT NUMBER: 143:115550

TITLE: Preparation of heterocyclic compounds as
selective

norepinephrine reuptake inhibitors for
treating hot flashes, impulse control

disorders and

personality change due to a general medical

condition

INVENTOR(S):

Allen, Albert John; Hemrick-Luecke, Susan;

Sumner,

Calvin Russell; Wallace, Owen Brendan

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE:

PCT Int. Appl., 337 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

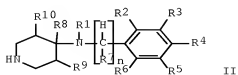
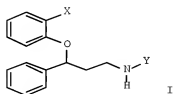
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005060949	A2	20050707	WO 2004-US38221	
20041201				
WO 2005060949	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,				
CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				

GB, GD,
 KZ, LC,
 NA, NI,
 SL, SY,
 ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM,
 DE, DK,
 PL, PT,
 GW, ML,
 MR, NE, SN, TD, TG
 CA 2548304 A1 20050707 CA 2004-2548304
 20041201
 EP 1729754 A2 20061213 EP 2004-811076
 20041201
 EP 1729754 B1 20080702
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE,
 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
 CN 1889940 A 20070103 CN 2004-80036841
 20041201
 JP 2007513945 T 20070531 JP 2006-543830
 20041201
 AT 399557 T 20080715 AT 2004-811076
 20041201
 ES 2307071 T3 20081116 ES 2004-811076
 20041201
 US 20070015786 A1 20070118 US 2006-581015
 20060530
 KR 2006121178 A 20061128 KR 2006-711571
 20060612
 PRIORITY APPLN. INFO.: US 2003-529428P P
 20031212 WO 2004-US38221 W
 20041201
 OTHER SOURCE(S): CASREACT 143:115550; MARPAT 143:115550
 GI



AB The invention relates to a method of preventing or treating hot flashes, vasomotor symptoms, impulse control disorders or personality change due to a general medical condition, comprising administering to a patient in need thereof a therapeutically effective amount of a selective norepinephrine reuptake inhibitor selected from atomoxetine, reboxetine, I [X = alkylthio; Y = alkyl], II [n = 1-3; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2-R4 = H, alkyl, alkoxy, etc.; R5-R6 = H, alkyl, alkoxy, halo; R7-R8 = H, alkyl; R9-R10 = H, halo, OH, CN, alkyl, alkoxy], etc. Over 200 title compds. such as I, II and other heterocyclic compds. disclosed, were prepared E.g., a 2-step synthesis of N-(2-methylpropyl)-N-[(2-fluorophenyl)methyl]piperidin-4-amine fumarate, starting from tert-Bu 4-(2-methylpropylamino)piperidine-1-carboxylate and 2-fluorobenzaldehyde, was given. The preferred exemplified title compds. exhibit a Ki value less than 1 μ M, more preferably less than 500 nM at the norepinephrine transporter as determined using the scintillation proximity assay.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L36 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2009 ACS ON STM
 ACCESSION NUMBER: 2005:523264 CAPLUS Full-text
 DOCUMENT NUMBER: 143:59831
 TITLE: A preparation of aminopiperidine derivatives, useful for the treatment of cognitive failure
 INVENTOR(S): Hatfield, Alan Kramer; Bymaster, Franklin Porter;
 McKinzie, David Lee; Tucker, Tina Marie;
 Keaffaber, Kirk Matthew; Sumner, Calvin Russell;
 Trzepacz, Paula Terese; Allen, Albert John; Kelsey, Douglas
 Kenneth; Michelson, David; Gehlert, Donald Richard;
 Yang, Charles Renkin
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 300 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053663	A2	20050616	WO 2004-US37195	
20041124				
WO 2005053663	A3	20050811		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,			

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 NA, NI, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
 SL, SY, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
 ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL,
 PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
 ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

20031124

US 2003-524450P

P

US 2003-524781P

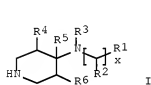
P

20031125

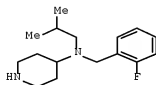
OTHER SOURCE(S):

MARPAT 143:59831

GI



I



II

AB The invention relates to a preparation of aminopiperidine derivs.
 of formula I [wherein: x is 1-3; R1 is (un)substituted phenyl; R2
 and R5 are independently H or alkyl; R3 is (cyclo)alkyl, alkenyl,
 or cycloalkylalkyl, etc.; R4 is H, halogen, or OH, etc.; R6 is H,
 halogen, CN, or alkyl, etc.], useful for the treatment of
 cognitive failure. Selective norepinephrine reuptake inhibitors
 were used to treat cognitive failure. For instance, fumarate salt
 of aminopiperidine derivative II was prepared via imination of 2-
 fluorobenzaldehyde by tert-Bu 4-[(2-methylpropyl)amino]piperidine-
 1-carboxylate, reduction of the obtained imine, and subsequent
 fumaric acid salt formation. The preferred invention compds.
 exhibit Ki values less than 500 nM at the norepinephrine
 transporter.

L36 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:

2005:451370 CAPLUS [Full-text](#)

DOCUMENT NUMBER:

142:482071

TITLE:

Preparation of morpholine derivatives as
 norepinephrine reuptake inhibitors

INVENTOR(S):

Campbell, Gordon Iain; Cases-Thomas, Manuel

Javier;

Helene

PATENT ASSIGNEE(S):

SOURCE:

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

Man, Teresa; Masters, John Joseph; Rudyk,

Catherine Eugenie; Walter, Magnus Wilhelm

Eli Lilly and Company, USA

PCT Int. Appl., 133 pp.

CODEN: PIXXD2

Patent

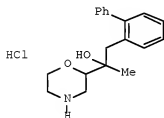
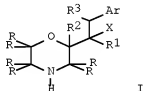
English

1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005047272	A1	20050526	WO 2004-US32771	
20041028				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,				
CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				
GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				
SL, SY,				
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,				
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,				
RO, SE,				
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,				
MR, NE,				
SN, TD, TG				
AU 2004289616	A1	20050526	AU 2004-289616	
20041028				
CA 2544649	A1	20050526	CA 2004-2544649	
20041028				
EP 1682523	A1	20060726	EP 2004-794209	
20041028				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,				
PL, SK, HR				
CN 1878762	A	20061213	CN 2004-80033115	
20041028				
BR 2004015273	A	20061219	BR 2004-15273	
20041028				
JP 2007510720	T	20070426	JP 2006-539492	
20041028				
US 20070083046	A1	20070412	US 2006-577841	
20060429				
US 7423037	B2	20080909		

MX 2006005226	A	20060720	MX 2006-5226	
20060509				
KR 2006086408	A	20060731	KR 2006-708999	
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KR 783855	B1	20071210		
NO 2006002700	A	20060808	NO 2006-2700	
20060612				
PRIORITY APPLN. INFO.:			GB 2003-26148	A
20031110				
20040109			US 2004-535459P	P
			WO 2004-US32771	W
20041028				
OTHER SOURCE(S):		CASREACT 142:482071; MARPAT 142:482071		
GI				



AB Title compds. I [X = OH, alkoxy, NH₂, etc.; R independently = H, alkyl, with provisions; R₁ = (un)substituted-alkyl, -alkoxy, CN, etc.; R₂ = H, alkyl; R₃ = H, alkyl; Ar = (un)substituted-Ph, -5- to 6-membered heteroaryl] and their pharmaceutically acceptable salts, are prepared and disclosed as norepinephrine reuptake inhibitors. Thus, e.g., II was prepared by conversion of 4-benzyl-morpholine-2-carbonitrile into the resp. carboxylic Et ester followed by amidation with N,N-dimethylhydroxylamine and subsequent Grignard reactions with Me magnesium bromide and 2-phenylbenzyl magnesium bromide followed by debenzoylation and conversion into the HCl salt. The activity of I was evaluated in a CYP2D6 inhibition assay and preferred compds. of the invention exhibited an IC₅₀ higher than 6 μ M. I as norepinephrine reuptake inhibitors should prove useful in the treatment of disorders that

are associated with norepinephrine dysfunction. Pharmaceutical
 compns. comprising I are disclosed.
 REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L36 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:216719 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291416
 TITLE: Treatment of stuttering and other
 communication disorders with norepinephrine reuptake
 inhibitors
 INVENTOR(S): Kelsey, Douglas Kenneth
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 299 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021095	A2	20050310	WO 2004-US25591	
20040825				
WO 2005021095	A3	20050609		
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,				
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SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,				
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CA 2532349	A1	20050310	CA 2004-2532349	
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US 20070032554
20060214
PRIORITY APPLN. INFO.:
20030827

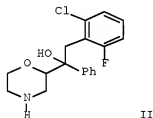
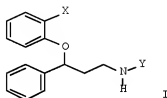
A1 20070208

MARPAT 142:291416

US 2006-568269

US 2003-498018P P
WO 2004-US25591 W

20040825
OTHER SOURCE(S):
GI



AB Provided are methods and medicaments for treating stuttering or another communication disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone with 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation. The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

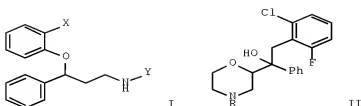
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE

ACCESSION NUMBER: 2005:216660 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291415
 TITLE: Treatment of pervasive development disorders
 employing
 noradrenaline reuptake inhibitors
 INVENTOR(S): Allen, Albert John; Kelsey, Douglas Kenneth
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 300 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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20040825	WO 2005020976	A2	20050310	WO 2004-US25593	
	WO 2005020976	A3	20050616		
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
20040825	CA 2536161	A1	20050310	CA 2004-2536161	
20040825	EP 1660065	A2	20060531	EP 2004-780431	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 20060241188	A1	20061026	US 2006-568466	
20060214					
PRIORITY APPLN. INFO.:				US 2003-498146P	P
20030827				WO 2004-US25593	W
20040825					
OTHER SOURCE(S):				CASREACT 142:291415; MARPAT 142:291415	
GI					



AB Provided are methods and medicaments for treating a pervasive development disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl (R = H) was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone by 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation of the obtained alc. I (R = Bn). The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

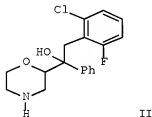
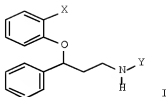
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE

L36 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:216659 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 142:291414
 TITLE: Treatment of learning disabilities and motor skills
 disorder with norepinephrine reuptake inhibitors
 INVENTOR(S): Sumner, Calvin Russell
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 304 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020975	A2	20050310	WO 2004-US25592	
20040825				

WO 2005020975 A3 20050602
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 GB, GD,
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 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
 ZM, ZW
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 ZW, AM,
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 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
 RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE,
 SN, TD, TG
 CA 2530014 A1 20050310 CA 2004-2530014
 20040825
 EP 1660064 A2 20060531 EP 2004-780430
 20040825
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
 US 20070105960 A1 20070510 US 2006-568244
 20060214
 PRIORITY APPLN. INFO.: US 2003-498019P P
 20030827 WO 2004-US25592 W
 20040825
 OTHER SOURCE(S): MARPAT 142:291414
 GI



AB Provided are methods and medicaments for treating a learning disability or a motor skills disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone with 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation. The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

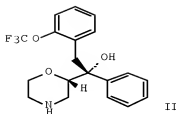
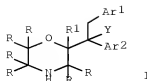
L36 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:1036891 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 142:16841
 TITLE: Treatment of emotional dysregulation
 INVENTOR(S): Allen, Albert John; Cloutier, Kathleen Ann; Michelson,
 David; Reimherr, Frederick William
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 155 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
20040511	A2	20041202	WO 2004-US13005	
WO 2004103356	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2003-470752P	P
20030515				
OTHER SOURCE(S):		MARPAT 142:16841		
AB		Provided is a method of treating emotional dysregulation comprising administering to a patient in need of such treatment a selective norepinephrine reuptake inhibitor.		
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS		
		RECORD. ALL CITATIONS AVAILABLE IN THE		
RE FORMAT				
L36 ANSWER 14 OF 15	CAPLUS	COPYRIGHT 2009 ACS on STN		
ACCESSION NUMBER:	2004:182855	CAPLUS Full-text		
DOCUMENT NUMBER:	140:217649			
TITLE:	Preparation of aryl and heteroaryl morpholine derivatives as norepinephrine reuptake inhibitors			
INVENTOR(S):	Cases-Thomas, Manuel Javier; Houghton, Helen Louise;			
Sivi;	Lamas-Peteira, Carlos; Ouwerkerk-Mahadevan,			
Rudyk,	Masters, John Joseph; Simmonds, Robin George;			
Wilhelm	Helene Catherine Eugenie; Walter, Magnus			
PATENT ASSIGNEE(S):	Eli Lilly and Company, USA			
SOURCE:	PCT Int. Appl., 82 pp.			
	CODEN: PIXXD2			

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018441	A1	20040304	WO 2003-US23270	
20030818				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003268024	A1	20040311	AU 2003-268024	
20030818				
EP 1534694	A1	20050601	EP 2003-748975	
20030818				
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 20060003998	A1	20060105	US 2005-524921	
20050215				
US 7354920	B2	20080408		
PRIORITY APPLN. INFO.:			GB 2002-19687	A
20020823				
20021001			US 2002-415303P	P
			WO 2003-US23270	W
20030818				
OTHER SOURCE(S):	MARPAT 140:217649			
GI				



AB Morpholine derivs. of formula I [R = independently H, alkyl; R1 = H, alkyl; Y = OH, alkoxy; Ar1, Ar2 = (substituted) Ph, (substituted) heteroaryl] are prepared. The compds. are selective inhibitors of the reuptake of norepinephrine. Thus, II.HCl was prepared from (4-benzylmorpholin-2-yl)-phenylmethanone (preparation given) and 2-(trifluoromethoxy)benzyl bromide. The compds. had Ki values less than 500 nM at the norepinephrine transporter in a scintillation proximity assay.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L36 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:182714 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:235724

TITLE: Preparation of benzyl morpholine derivatives capable

of selectively inhibiting norepinephrine reuptake

INVENTOR(S): Walter, Magnus Wilhelm; Clark, Barry Peter; Gallagher,

Peter Thaddeus; Haughton, Helen Louise; Rudyk,

Helene

Catherine Eugenie

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

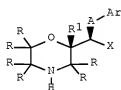
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

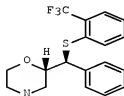
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017977	A2	20040304	WO 2003-US23269	
20030818				
WO 2004017977	A3	20040401		
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 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG AU 2003269923 A1 20040311 AU 2003-269923
 20030818 EP 1534291 A2 20050601 EP 2003-751812
 20030818 EP 1534291 B1 20081112
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 AT 413882 T 20081115 AT 2003-751812
 20030818 US 20060035894 A1 20060216 US 2005-524650
 20050217 US 7384941 B2 20080610
 PRIORITY APPLN. INFO.: GB 2002-19690 A
 20020823 US 2002-415328P P
 20021001 WO 2003-US23269 W
 20030818
 OTHER SOURCE(S): MARPAT 140:235724
 GI



I



II

AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl group, a cycloalkyl group or cycloalkylmethyl group] and

pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared via substitution of (2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (preparation given) with 2-trifluoromethylthiophenol with subsequent debenzoylation. I have been found to exhibit a Ki value less than 500nM at the norepinephrine transporter as determined by scintillation proximity assays. In addition, I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l32 and (neuro? or anti!depress? or anti!psycho? or mental?)

194 L32
628328 NEURO?
0 ANTI!DEPRESS?
1 ANTI!PSYCHO?
66797 MENTAL?

L37 17 L32 AND (NEURO? OR ANTI!DEPRESS? OR ANTI!PSYCHO? OR MENTAL?)

=> d l37 ibib abs 10-17

L37 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:605280 CAPLUS Full-text
DOCUMENT NUMBER: 145:83221
TITLE: Preparation of bridged arylpiperidines as nk1 antagonists
INVENTOR(S): Xiao, Dong; Palani, Anandan; Wang, Cheng; Tsui,
Hon-Chung; Huang, Xianhai; Shah, Sapna S.; Rao, Ashwin
U.; Chen, Xiao; Paliwal, Sunil; Shih, Neng-Yang
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006065654	A1	20060622	WO 2005-US44647	
20051207				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,			

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 UZ, VC, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
 VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
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 BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 US 20060258665 A1 20061116 US 2005-291363
 20051201
 US 7354922 B2 20080408
 CA 2591079 A1 20060622 CA 2005-2591079
 20051207
 EP 1828188 A1 20070905 EP 2005-849677
 20051207
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 JP 2008523144 T 20080703 JP 2007-546775
 20051207
 MX 200707152 A 20070814 MX 2007-7152
 20070614
 CN 101115753 A 20080130 CN 2005-80048054
 20070813
 PRIORITY APPLN. INFO.: US 2004-635971P P
 20041214 WO 2005-US44647 W
 20051207
 OTHER SOURCE(S): MARPAT 145:83221
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. I [Arl-2 independently = (un)substituted aryl or heteroaryl; X1 = O, NH, N-alkyl, N-haloalkyl, etc.; X2 = O, CH2, C(alkyl)2, NH, N-alkyl, etc.; X3 = CO, CH2, C(alkyl)2, C(=N-alkyl), etc.; X4 = NH, N-alkyl, CH2, etc.; with provision that when X3 = (un)substituted C, at least one of X2 and X4 also equal (un)substituted C; n = 0-4; R1 = H, OH, (un)substituted alkyl, etc.; R2-5 independently = H, haloalkyl, cycloalkyl, etc.; further provisions allow for when X2 = N the substituent on N may together with R1 form a (un)substituted ring], and their pharmaceutically acceptable salts, were prepared and disclosed as useful in

treating diseases or conditions mediated by NK1 receptors, for example various physiol. disorders, symptoms or diseases, including emesis, depression, anxiety and cough. Thus, e.g., II was prepared in a multistep synthesis from III. Especially preferred compds. of the invention have Ki values of 0.05 nM to about 1 nM for the NK1 receptor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:365001 CAPLUS Full-text

DOCUMENT NUMBER: 144:432692

TITLE: Preparation of diaminoalkanes, particularly N-(1-aminopropan-2-yl)piperidine-1-

carboxamides, as

aspartic protease inhibitors

INVENTOR(S): Baldwin, John J.; Claremon, David A.; Tice, Colin;

Cacatian, Salvation; Dillard, Lawrence W.;

Ishchenko,

Alexey V.; Yuan, Jing; Xu, Zhenrong; McGeehan,

Gerard;

Zhao, Wei; Simpson, Robert D.; Singh, Suresh

B.;

Flaherty, Patrick T.; Wery, Jean-Pierre

PATENT ASSIGNEE(S): Vitae Pharmaceutical, Inc, USA

SOURCE: PCT Int. Appl., 755 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006042150	A1	20060420	WO 2005-US36230	
20051007				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,			

alkylaminosulfonylamino, (un)substituted phenylamino, heteroaryl amino; A = (un)saturated (un)substituted 4- to 7-membered ring, which is optionally bridged by (CH₂)_m via bonds to 2 members of said ring; Q and Y are attached to C or N atoms in ring A in a 1,2 or 1,3 or 1,4 relationship; Q = divalent radical selected from CO, C:S, SO₂, CO-CO, CO-CH₂-CO, etc.; m = 1-3; R₄ = H, halo/alkoxy/cyano/alkyl; L = (un)substituted linear (C2-C4)alkyl chain when G = OH, OR₉, NH₂, NHR₉, NR₉R₁₀, NHC(:NH)NH₂, or NHC(:NH)NHR₉; or L = (un)substituted linear (C1-C3)alkyl chain when G = C(:NH)NH₂, or C(:NH)NHR₉; G = OH, OR₉, NH₂, NHR₉, NR₉R₁₀, NHC(:NH)NH₂, NHC(:NH)NHR₉, C(:NH)NH₂, C(:NH)NHR₉; R₉ = halo/alkyl, (un)substituted Ph, naphthyl, heteroaryl, heteroarylsulfinyl, naphthyl, etc.; R₁₀ = halo/alkyl; with provisos;), and their enantiomers, diastereomers, and salts, e.g. II, which are orally active and bind to aspartic proteases to inhibit their activity. I are useful in the treatment or amelioration of diseases associated with elevated levels of aspartic protease activity. Thus, reacting benzyl N-((S)-2-amino-3-cyclohexylpropyl)-N-(2,2,2-trifluoroethyl)carbamate (preparation given) with (1S)-1-(3-chlorophenyl)-5-methoxy-1-((3R)-piperidin-3-yl)pentan-1-ol and CDI in the presence of DIEA in CH₂Cl₂, followed by Cbz-deprotection gave piperidine II. Selected I had an IC₅₀ in the range of 0.001 nM to 5 nM for the inhibition of renin activity. I are useful in ameliorating or treating aspartic protease related disorders, such as hypertension, congestive heart failure, cardiac hypertrophy, cardiac fibrosis, etc. cardiomyopathy postinfarction, nephropathy, vasculopathy and neuropathy, diseases of the coronary vessels.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L37 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1176480 CAPLUS Full-text

DOCUMENT NUMBER: 143:440426

TITLE: Substituted morpholine compounds for the treatment of

central nervous system disorders, their

preparation

and pharmaceutical compositions

INVENTOR(S):

Barta, Nancy S.; Glase, Shelly Ann; Gray,

David L.;

Reichard, Gregory A.; Simons, Lloyd J.; Xu,

Weijan

PATENT ASSIGNEE(S):

Warner-Lambert Company LLC, USA

SOURCE:

U.S. Pat. Appl. Publ., 85 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050245519	A1	20051103	US 2005-119210	

20050429				
AU 2005238296	A1	20051110	AU 2005-238296	
20050419				
CA 2564994	A1	20051110	CA 2005-2564994	
20050419				
WO 2005105763	A1	20051110	WO 2005-IB1158	
20050419				
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KR, KZ,				
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SK, SL,				
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MR, NE, SN, TD, TG				
EP 1745029	A1	20070124	EP 2005-733459	
20050419				
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IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR,				
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HR, LV, MK, YU				
CN 1950348	A	20070418	CN 2005-80013776	
20050419				
BR 2005010453	A	20071030	BR 2005-10453	
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JP 2007535530	T	20071206	JP 2007-510153	
20050419				
JP 4185154	B2	20081126		
NL 1028924	A1	20051101	NL 2005-1028924	
20050429				
NL 1028924	C2	20060427		
IN 2006DN05782	A	20070803	IN 2006-DN5782	
20061005				
MX 2006012505	A	20061215	MX 2006-12505	
20061027				
KR 2007006881	A	20070111	KR 2006-722767	
20061030				
NO 2006005456	A	20070104	NO 2006-5456	
20061127				
JP 2008019267	A	20080131	JP 2007-233201	
20070907				
PRIORITY APPLN. INFO.:			US 2004-567244P	P

20040430

JP 2007-510153 A3

20050419

WO 2005-IB1158 W

20050419

OTHER SOURCE(S): CASREACT 143:440426; MARPAT 143:440426

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB The invention relates to compds. of the formula I, which can be used in the treatment of central nervous system disorders. In compds. I, A is O or S; X is C1-10 alkyl, C2-8 alkenyl, aryl, heterocyclyl, C1-6 alkoxy, etc., with each group optionally substituted; and R1 - R5 are independently selected from H, OH, halo, C1-6 alkyl, aryl, C3-8 cycloalkyl, C2-6 alkenyl, C1-6 alkoxy, aryloxy, heterocyclyl, etc.; including pharmaceutically acceptable salts, enantiomers and diastereomers. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of central nervous system disorders. Ring opening of (R,R)-phenylglycidol with 1-naphthol followed by silylation of the primary alc., mesylation of the secondary alc., and desilylation gave mesylate II, which underwent ring closure to the epoxide, ring opening with ammonium hydroxide and amidation with chloroacetyl chloride, resulting in the formation of amide III. Compound III was converted to the morpholine by intramol. cyclization and Red-Al reduction to give morpholine IV. Several compds., e.g., IV, express high inhibition of human norepinephrine transporter (hNET) and human serotonin transporter (hSERT).

L37 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:588645 CAPLUS Full-text

DOCUMENT NUMBER: 143:115550

TITLE: Preparation of heterocyclic compounds as
selective

norepinephrine reuptake inhibitors for

treating hot

personality flashes, impulse control disorders and

change due to a general medical condition

INVENTOR(S): Allen, Albert John; Hemrick-Luecke, Susan;

Sumner,

Calvin Russell; Wallace, Owen Brendan

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 337 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

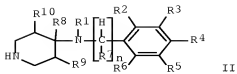
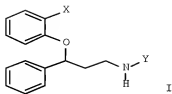
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005060949	A2	20050707	WO 2004-US38221	
20041201				
WO 2005060949	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2548304	A1	20050707	CA 2004-2548304	
20041201				
EP 1729754	A2	20061213	EP 2004-811076	
20041201				
EP 1729754	B1	20080702		
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CN 1889940	A	20070103	CN 2004-80036841	
20041201				
JP 2007513945	T	20070531	JP 2006-543830	
20041201				
AT 399557	T	20080715	AT 2004-811076	
20041201				
ES 2307071	T3	20081116	ES 2004-811076	
20041201				
US 20070015786	A1	20070118	US 2006-581015	
20060530				
KR 2006121178	A	20061128	KR 2006-711571	
20060612				
PRIORITY APPLN. INFO.:			US 2003-529428P	P
20031212				
			WO 2004-US38221	W
20041201				
OTHER SOURCE(S):	CASREACT 143:115550; MARPAT 143:115550			
GI				



AB The invention relates to a method of preventing or treating hot flashes, vasomotor symptoms, impulse control disorders or personality change due to a general medical condition, comprising administering to a patient in need thereof a therapeutically effective amount of a selective norepinephrine reuptake inhibitor selected from atomoxetine, reboxetine, I [X = alkylthio; Y = alkyl], II [n = 1-3; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2-R4 = H, alkyl, alkoxy, etc.; R5-R6 = H, alkyl, alkoxy, halo; R7-R8 = H, alkyl; R9-R10 = H, halo, OH, CN, alkyl, alkoxy], etc. Over 200 title compds. such as I, II and other heterocyclic compds. disclosed, were prepared E.g., a 2-step synthesis of N-(2-methylpropyl)-N-[(2-fluorophenyl)methyl]piperidin-4-amine fumarate, starting from tert-Bu 4-(2-methylpropylamino)piperidine-1-carboxylate and 2-fluorobenzaldehyde, was given. The preferred exemplified title compds. exhibit a K_i value less than 1 μM , more preferably less than 500 nM at the norepinephrine transporter as determined using the scintillation proximity assay.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

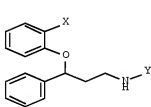
RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

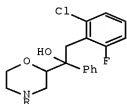
L37 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:216660 CAPLUS Full-text
 DOCUMENT NUMBER: 142:291415
 TITLE: Treatment of pervasive development disorders employing norepinephrine reuptake inhibitors
 INVENTOR(S): Allen, Albert John; Kelsey, Douglas Kenneth
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 300 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020976	A2	20050310	WO 2004-US25593	
20040825				
WO 2005020976	A3	20050616		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,			
CA, CH,	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,			

GB, GD,
 KZ, LC,
 NA, NI,
 SL, SY,
 ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM,
 DE, DK,
 RO, SE,
 MR, NE,
 SN, TD, TG
 CA 2536161 A1 20050310 CA 2004-2536161
 20040825
 EP 1660065 A2 20060531 EP 2004-780431
 20040825
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
 US 20060241188 A1 20061026 US 2006-568466
 20060214
 PRIORITY APPLN. INFO.: US 2003-498146P P
 20030827 WO 2004-US25593 W
 20040825
 OTHER SOURCE(S): CASREACT 142:291415; MARPAT 142:291415
 GI



I



II

AB Provided are methods and medicaments for treating a pervasive development disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs.

(as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl (R = H) was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone by 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation of the obtained alc. I (R = Bn). The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L3/ ANSWER 15 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:1036891 CAPLUS Full-text
 DOCUMENT NUMBER: 142:16841
 TITLE: Treatment of emotional dysregulation
 INVENTOR(S): Allen, Albert John; Cloutier, Kathleen Ann; Michelson,
 David; Reimherr, Frederick William
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 155 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
2004103356	A2	20041202	WO 2004-US13005	
20040511				
WO 2004103356	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:		US 2003-470752P	P	
20030515				

OTHER SOURCE(S): MARPAT 142:16841
 AB Provided is a method of treating emotional dysregulation comprising administering to a patient in need of such treatment a selective norepinephrine reuptake inhibitor.

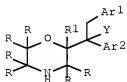
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

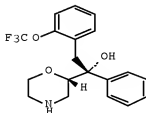
L37 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:182855 CAPLUS Full-text
 DOCUMENT NUMBER: 140:217649
 TITLE: Preparation of aryl and heteroaryl morpholine derivatives as norepinephrine reuptake inhibitors
 INVENTOR(S): Cases-Thomas, Manuel Javier; Haughton, Helen Louise;
 Sivi; Lamas-Peteira, Carlos; Ouwerkerk-Mahadevan, Masters, John Joseph; Simmonds, Robin George; Rudyk, Helene Catherine Eugenie; Walter, Magnus Wilhelm
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 82 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004018441	A1	20040304	WO 2003-US23270	
20030818				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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AU 2003268024	A1	20040311	AU 2003-268024	
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EP 1534694 A1 20050601 EP 2003-748975
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 US 20060003998 A1 20060105 US 2005-524921
 20050215 B2 20080408
 US 7354920 GB 2002-19687 A
 PRIORITY APPLN. INFO.: US 2002-415303P P
 20020823 WO 2003-US23270 W
 20021001
 20030818
 OTHER SOURCE(S): MARPAT 140:217649
 GI



I



II

AB Morpholine derivs. of formula I [R = independently H, alkyl; R1 = H, alkyl; Y = OH, alkoxy; Ar1, Ar2 = (substituted) Ph, (substituted) heteroaryl] are prepared. The compds. are selective inhibitors of the reuptake of norepinephrine. Thus, II.HCl was prepared from (4-benzylmorpholin-2-yl)-phenylmethanone (preparation given) and 2-(trifluoromethoxy)benzyl bromide. The compds. had Ki values less than 500 nM at the norepinephrine transporter in a scintillation proximity assay.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:182714 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 140:235724
 TITLE: Preparation of benzyl morpholine derivatives
 capable of selectively inhibiting norepinephrine
 reuptake
 INVENTOR(S): Walter, Magnus Wilhelm; Clark, Barry Peter;
 Gallagher, Peter Thaddeus; Haughton, Helen Louise; Rudyk,
 Helene

PATENT ASSIGNEE(S):
 SOURCE:
 DOCUMENT TYPE:
 LANGUAGE:
 FAMILY ACC. NUM. COUNT:
 PATENT INFORMATION:

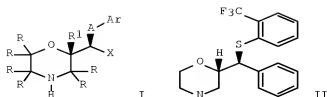
Catherine Eugenie
 Eli Lilly and Company, USA
 PCT Int. Appl., 81 pp.
 CODEN: PIXXD2

Patent
 English

1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	WO 2004017977	A3	20040401		
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TM, TN,	PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,				
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20030818	AT 413882	T	20081115	AT 2003-751812	
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OTHER SOURCE(S):					
GI					

MARPAT 140:235724



AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl group, a cycloalkyl group or cycloalkylmethyl group] and pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared via substitution of (2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (preparation given) with 2-trifluoromethylthiophenol with subsequent debenzoylation. I have been found to exhibit a Ki value less than 500nM at the norepinephrine transporter as determined by scintillation proximity assays. In addition, I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l32 and hormon?
194 L32
450103 HORMON?
L38 9 L32 AND HORMON?

=> d l38 ibib abs 1-9

L38 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:322517 CAPLUS [Full-text](#)
DOCUMENT NUMBER: 137:140761
TITLE: Synthesis, bioassay and NMR study of methyleneoxy isosters of oxytocin and vasopressin
AUTHOR(S): Marik, Jan; Budesinsky, Milos; Slaninova, Jirina;
CORPORATE SOURCE: Hlavacek, Jan
Biochemistry, Institute of Organic Chemistry and
Academy of Sciences of the Czech Republic,
Prague, 16610/6, Czech Rep.

SOURCE: Collection of Czechoslovak Chemical
Communications

(2002), 67(3), 373-392
CODEN: CCCCCAK; ISSN: 0010-0765

PUBLISHER: Institute of Organic Chemistry and
Biochemistry,

Academy of Sciences of the Czech Republic

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:140761

AB Syntheses of pseudodipeptides H-Tyr ψ [CH₂O]Ile-OH and H-Tyr ψ [CH₂O]Phe-OH were carried out using the intramol. Williamson reaction of O-benzyltyrosinol with Et chloroacetate followed by N-protection and aldol reaction of the corresponding morpholin-3-one in position C2 with butanone or benzaldehyde, elimination of the hydroxy group to give derivs. with a double bond either as the E/Z (1 : 1) diastereomeric mixture in the case of the former derivative or as the Z-isomer only in the case of the latter one. Stereoselective hydrogenation and hydrolysis of both the lactams yielded the corresponding pseudodipeptides lacking the carbonyl group as a hydrogen bond donor. The introduction of the pseudodipeptides into positions 2 and 3 of oxytocin and vasopressin caused total absence of all biol. activities in the formed analogs. The results of the bioassay and NMR study confirmed the importance of the H-bond between the backbone carbonyl of the Tyr2 and NH proton of the Asn5 residues for stabilization of the β -turn in the cyclic hexapeptide part of both the hormones and for their biol. activity.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L38 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:314504 CAPLUS Full-text

DOCUMENT NUMBER: 135:119630

TITLE: Ginsenoside production in different phenotypes
of

Panax ginseng transformed roots

AUTHOR(S): Mallol, A.; Cusido, R. M.; Palazon, J.;
Bonfill, M.;

Morales, C.; Pinol, M. T.

CORPORATE SOURCE: Facultad de Farmacia, Seccion de Fisiologia
Vegetal,

Universidad de Barcelona, Barcelona, 08028,

Spain

SOURCE: Phytochemistry (2001), 57(3), 365-371

CODEN: PYTCAS; ISSN: 0031-9422

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Transformed roots were obtained after the inoculation of sterile root disks of Panax ginseng C.A. Meyer with Agrobacterium rhizogenes A4. The established hairy root lines displayed three morphol. phenotypes when cultured on hormone-free liquid Schenk and Hildebrandt medium. Most of the cultures showed the

characteristic traits of hairy roots (HR-M), while others were either callus-like (C-M) or thin (T-M) without branching. The growth rate of the transformed root lines was always higher than that of untransformed roots, showing that the genetic changes caused by the *A. rhizogenes* transformation conditioned a higher biomass formation. When considering the different transformed root phenotypes, we can observe that the highest ginsenoside production was achieved by HR-M root lines, closely followed by C-M ones, whereas the lowest yield was reached by T-M root phenotype. The study of the integration of the T1-DNA and TR-DNA fragments of the pRiA4 in the root genome showed that the *aux1* gene was always detected in HR-M and C-M root phenotypes which presented the highest biomass and ginsenoside productions. This fact suggests a significant role of aux genes in the morphol. of *Panax ginseng* transformed roots. The ginsenoside pattern of transformed roots varied according to their morphol., although the ginsenoside contents of the Rg group was always higher than that of the Rb group. From our results, we can infer the potential of some root phenotypes of *Panax ginseng* hairy root cultures for an improved ginsenoside production. Transformed roots of *Panax* showed several phenotypes and different capacity to produce triterpenic saponines. Root phenotype depends on T-DNA fragments integrated into the plant genome.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L38 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:1437 CAPLUS Full-text

DOCUMENT NUMBER: 116:1437

ORIGINAL REFERENCE NO.: 116:295a,298a

TITLE: *Agrobacterium rhizogenes* mediated transformation of

the forage legumes *Medicago sativa* and

Onobrychis

viciifolia

AUTHOR(S): Golds, T. J.; Lee, J. Y.; Husnain, T.; Ghose, T. K.;

Davey, M. R.

CORPORATE SOURCE: Dep. Bot., Univ. Nottingham, Nottingham, NG7 2RD, UK

SOURCE: Journal of Experimental Botany (1991), 42(242),

1147-57

CODEN: JEBOA6; ISSN: 0022-0957

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three cultivars of *M. sativa* and one cultivar of *O. viciifolia* were evaluated for their response to inoculation with *A. rhizogenes* strain A4T (containing pRiA4b). A cultivar-dependent response was observed in *M. sativa* with 94%, 25%, and 4% of infected stem explants producing transformed roots in the cultivars Vertus, Regen-S, and Rangelander, resp. In *O. viciifolia* cv. Hampshire Giant, an explant-dependent response was observed with 78% and 50% of seedling cotyledon and hypocotyl explants responding, resp. Leaf explants failed to produce

transformed roots. Transformed roots showed plagiotropic and neg. geotropic growth on hormone-free agar MS medium. Production of transgenic shoots from *O. viciifolia* root cultures occurred spontaneously. Recovery of transgenic plants from *M. sativa* cv. Rangelander was achieved by transfer of callus (induced on UM medium containing 2.0 mg dm-3 2,4-D and 0.25 mg dm-3 kinetin) to MS medium containing 0.5 mg dm-3 BAP and 0.05 mg dm-3 NAA. Cultured roots of both species synthesized opines (agropine and mannopine). Extensive morphol. variation was observed in plants of *M. sativa* (clone A1) and *O. viciifolia* A4T1 established in the glasshouse. DNA sequences homologous to TL-DNA and TR-DNA were present in root clones and regenerated plants.

L38 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1991:625102 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 115:225102

ORIGINAL REFERENCE NO.: 115:38223a,38226a

TITLE: Direct regeneration of transformed shoots in Brassica

napus from hypocotyl infections with

Agrobacterium

rhizogenes

AUTHOR(S): Damgaard, Ove; Rasmussen, Ole

CORPORATE SOURCE: Inst. Mol. Biol. Plant Physiol., Aarhus, DK-8000, Den.

SOURCE: Plant Molecular Biology (1991), 17(1), 1-8

CODEN: PMBIDB; ISSN: 0167-4412

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Genetically transformed root clones of rapeseed (*B. napus*) were obtained after in vitro infection of excised hypocotyl segments with a wild-type strain of *A. rhizogenes* and 2 strains of *A. rhizogenes* harboring kanamycin resistance. The ability of hairy root formation was affected by light and was highly dependent on the location of the infection site at the hypocotyl. Inoculation of decapitated hypocotyls with an intact root system gave rise to direct shoot formation from the site of inoculation. Histol. sections showed that several meristems were initiated at the inoculation site. Root and shoot clones were isolated and subcultured axenically in hormone-free liquid MS medium. Identification of transformed root and shoot clones was based on opine assays. Further selection was carried out in kanamycin-enriched medium. All opine-pos. root clones showed NPT II (neomycin phosphotransferase) activity. Nearly half of the shoot clones expressed a strong NPT II activity while the rest gave a weak or no NPT II response.

L38 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1991:18668 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 114:18668

ORIGINAL REFERENCE NO.: 114:3244h,3245a

TITLE: Agropine synthesis of a Ti-transformed tobacco line

AUTHOR(S): Inoguchi, Masahiko; Kamada, Hiroshi; Harada, Hiroshi

CORPORATE SOURCE: Inst. Biol. Sci., Univ. Tsukuba, Tsukuba, 305,
Japan
SOURCE: Journal of Plant Physiology (1990), 136(6),
680-4

CODEN: JPPHEY; ISSN: 0176-1617
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Agropine synthesis in a Ti-transformed tobacco (*Nicotiana tabacum* cv. Wisconsin 38) line was investigated in relation to tissue development. A teratoma was induced with *Agrobacterium tumefaciens* A66 and shoots were isolated in vitro. One of these showed agropine synthesis but without hormone autonomy. Southern blot anal. revealed that this line lacked the oncogenic genes of TL-DNA fragment but possessed a TR-DNA copy. Lack of oncogenic genes allowed plants to be regenerated repeatedly in vitro. Agropine content and synthetic activity of this transformant was consistently higher in callus tissues than in plant tissues.

L38 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1990:213982 CAPLUS Full-text

DOCUMENT NUMBER: 112:213982

ORIGINAL REFERENCE NO.: 112:36057a,36060a

TITLE: T-DNA presence and opine production in tumors
of *Picea*

abies (L.) Karst induced by *Agrobacterium tumefaciens*

A281
AUTHOR(S): Hood, Elizabeth E.; Clapham, David H.; Ekberg,
Inger;

Johannson, Thomas
CORPORATE SOURCE: Dep. For. Genet., Swed. Univ. Agric. Sci.,
Uppsala,

S-750 07, Swed.
SOURCE: Plant Molecular Biology (1990), 14(2), 111-17
CODEN: PMBIDB; ISSN: 0167-4412

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hypervirulent *A. tumefaciens* strain A281 formed frequent tumors (31%) on *P. abies* (Norway spruce). Three-month-old seedlings were inoculated and tumors were established that grew hormone-independently in culture. Tumors contained agropine and mannopine/mannopinic acid as determined by acid pH paper electrophoresis. In addition, DNA hybridization studies showed that the DNA from these tumor lines contained sequences homologous to Ti plasmid T-DNA, whereas wild-type spruce seedling DNA did not. *Agrobacterium* vectors may be of significance for gene transfer into this species.

L38 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1988:52902 CAPLUS Full-text

DOCUMENT NUMBER: 108:52902

ORIGINAL REFERENCE NO.: 108:8777a,8780a

TITLE: Saponin production by cultures of *Panax*
ginseng

transformed with *Agrobacterium rhizogenes*

AUTHOR(S): Yoshikawa, Takafumi; Furuya, Tsutomu
CORPORATE SOURCE: Sch. Pharm. Sci., Kitasato Univ., Tokyo, 108,
Japan
SOURCE: Plant Cell Reports (1987), 6(6), 449-53
CODEN: PCRPD8; ISSN: 0721-7714
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hairy root culture of ginseng (*P. ginseng*) was established after roots were induced on callus following infection with *A. rhizogenes*. The transformed cultures of ginseng could be subcultured as an axenic root culture in the absence of phytohormones, and grew with extensive lateral branches more rapidly than the ordinary cultured roots induced by hormonal control from ginseng callus. The hairy roots synthesized the same saponins, ginsenosides, as those of the native root, up to .apprx.2.4-fold the quantity, and up to .apprx.2-fold in comparison with that of ordinary cultured roots, on a dry weight basis.

L38 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1986:124148 CAPLUS Full-text
DOCUMENT NUMBER: 104:124148
ORIGINAL REFERENCE NO.: 104:19511a,19514a
TITLE: Independent integration and seed-transmission
of the

TR-DNA of the octopine Ti plasmid pTiAch5 in

Nicotiana

plumbaginifolia

AUTHOR(S): Czako, Mihaly; Marton, Laszlo
CORPORATE SOURCE: Inst. Plant Physiol., Hung. Acad. Sci.,
Szeged,

H-6701, Hung.

SOURCE: Plant Molecular Biology (1986), 6(2), 101-9
CODEN: PMBIDB; ISSN: 0167-4412
DOCUMENT TYPE: Journal
LANGUAGE: English

AB After cocultivation of diploid *N. plumbaginifolia* protoplasts with an octopine-type *Agrobacterium tumefaciens* strain (LBA 4013), putative transformants were selected for hormone-independent growth, and were tested for T-DNA markers. The number of transformants expressing only TL-DNA markers, i.e. phytohormone autotrophy and octopine synthase [74505-31-0], was an order of magnitude higher than that of the cell lines which were simultaneously pos. for both TL- and TR-DNA markers (the latter being mannopine [87084-52-4] and agropine [70699-77-3]). In 1 transformant, line number 101, only the TR-DNA markers were found. Not each of the TL-, or TR-DNA markers were expressed in each transformant resulting in a variety of phenotypes. It included the unorganized or the shoot-teratoma type of growth combined with the presence or absence of opines; e.g. agropine was absent from some of the transformants containing its precursor, mannopine. 5-Azacytidine did not induce agropine synthesis in these lines. Southern blot anal. showed that the TR-DNA region coding for agropine synthesis was rearranged or absent in 1 of these lines. Similar variation in the expression of agropine and mannopine production was observed in transformants obtained with the

leucinopine-type strain A281. From line 101 plants could be easily regenerated with the ability to synthesize agropine and mannopine. The segregation in the self-progeny fitted to a 3:1 ratio, indicating that the TR-DNA was carried by a single chromosome. The Southern blot anal. showed that only opine-pos. plants contained TR-DNA. It also confirmed the absence of the TL-DNA, demonstrating the independent integration of the TR-region of the octopine-type Ti plasmid pTiAch5.

L38 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1983:465311 CAPLUS Full-text

DOCUMENT NUMBER: 99:65311

ORIGINAL REFERENCE NO.: 99:10081a,10084a

TITLE: In vitro plant transformation systems using liposomes

and bacterial cocultivation

AUTHOR(S): Fraley, Robb T.; Horsch, Rob B.

CORPORATE SOURCE: Mol. Biol. Dep., Monsanto Co., St. Louis, MO, 63167,

USA

SOURCE: Basic Life Sciences (1983), 26(Genet. Eng.

Plants: Agric. Perspect.), 177-94

CODEN: BLFSBY; ISSN: 0090-5542

DOCUMENT TYPE: Journal

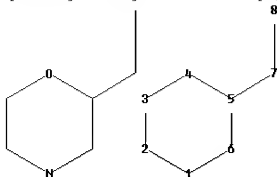
LANGUAGE: English

AB Conditions were developed for optimum phospholiposome-mediated tobacco mosaic virus RNA transfer into Petunia protoplasts. The concentration of the polyalc. solution used to stimulate liposome delivery was critical. Both polyethylene glycol (PEG) [25322-68-3] and polyvinylalc. [9002-89-5] gave comparable results at low concns., but PEG was more effective at high concns. High levels of CaCl₂ (5mM) stimulated delivery and virus production. This enhancement was mediated both by increased liposome binding to protoplasts and by stabilization of protoplast integrity by CaCl₂. Neutral pH and an incubation time of 5 min for the preincubation of liposomes and 20-30 min for the length of protoplast exposure to PEG also enhanced nucleic acid transfer. Cocultivation of Petunia protoplasts with *Agrobacterium tumefaciens* is also described. With a rapid plotting system and early selection for ~~hormone~~ autotrophy, transformation frequencies of 10-1 were observed with *A. tumefaciens* strains carrying octopine [34522-32-2]- nopaline [22350-70-5]- or agropine [~~70699-77-3~~]-type Ti plasmids. Most of the ~~hormone~~ -independent calluses (>90%) produced opines, and Southern hybridization confirmed the presence of T-DNA in several transformants. A high percentage (.apprx.1%) of the in vitro transformants were observed to shoot spontaneously while being passaged on ~~hormone~~-free medium. These shoots were transformed and produced high levels of octopine or nopaline. An important advantage of the high efficiency transformation is that the transformants can be identified by simply screening colonies for opine production in the absence of selective conditions.

<http://www.cas.org/support/stngen/stdoc/properties.html>

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chain nodes :

7 8

ring nodes :

1 2 3 4 5 6

chain bonds :

5-7 7-8

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

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exact bonds :

5-7 7-8

Match level :

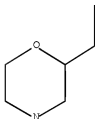
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L39 STRUCTURE UPLOADED

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L39 HAS NO ANSWERS

L39 STR



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 140 and (serotonin or ?epinephrin? or adrenergic? or dopamin?)

1457 L40
 76807 SEROTONIN
 53 SEROTONINS
 76812 SEROTONIN
 (SEROTONIN OR SEROTONINS)
 66707 ?EPINEPHRIN?
 78639 ADRENERGIC?
 107711 DOPAMIN?
 L41 54 L40 AND (SEROTONIN OR ?EPINEPHRIN? OR ADRENERGIC? OR
 DOPAMIN?)

=> s 140 and (central nervous system or CNS)
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 40 CENTRALS
 454870 CENTRAL
 (CENTRAL OR CENTRALS)
 241203 NERVOUS
 2736397 SYSTEM
 1472370 SYSTEMS
 3691088 SYSTEM
 (SYSTEM OR SYSTEMS)
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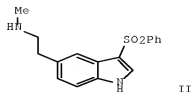
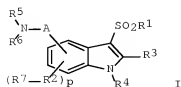
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=> d 143 ibib abs 1-6

L43 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2007:815018 CAPLUS Full-text
 DOCUMENT NUMBER: 147:211728
 TITLE: Preparation of sulfonyl substituted 1H-indoles
 as
 ligands for the 5-hydroxytryptamine receptors,
 particularly 5-HT6 and 5-HT2A receptors, and
 inhibitors of norepinephrine reuptake
 INVENTOR(S): McDevitt, Robert E.; Li, Yanfang; Robichaud,
 Albert
 J.; Heffernan, Gavin D.; Coghlan, Richard D.;
 Bernotas, Ronald C.
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
 SOURCE: PCT Int. Appl., 129pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007084841	A2	20070726	WO 2007-US60454	
20070112				

WO 2007084841 A3 20070913
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
AU 2007206016 A1 20070726 AU 2007-206016
20070112 CA 2636007 A1 20070726 CA 2007-2636007
20070112 US 20070203120 A1 20070830 US 2007-622649
20070112 EP 1973876 A2 20081001 EP 2007-710091
20070112 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
IN 2008DN05932 A 20081024 IN 2008-DN5932
20080708 NO 2008003057 A 20081003 NO 2008-3057
20080709 KR 2008114688 A 20081231 KR 2008-719566
20080808
PRIORITY APPLN. INFO.: US 2006-758833P P
20060113 WO 2007-US60454 W
20070112
OTHER SOURCE(S): MARPAT 147:211728
GI



AB Title compds. I [A = (un)substituted alkylene, alkenylene or alkynylene; R1 = (un)substituted alkyl, (hetero)cycloalkyl, (hetero)aryl, etc.; each R2 independently = bond, O, S, CO, C(O)O, etc.; R3 and R4 independently = H, (un)substituted alkyl, (hetero)cycloalkyl, (hetero)aryl, etc.; R5 and R6 independently = H, (un)substituted alkyl, haloalkyl, alkenyl, etc.; R5 and R6 may join together with N to form a 3- to 8-membered heterocycloalkyl ring or a 5- to 8-membered heteroaryl ring; each R7 independently = H, halo, CN, NO2, etc., p = 0-3], and their pharmaceutically acceptable salts, are prepared and disclosed as ligands for the 5-hydroxytryptamine (5-HT) receptors, especially 5-HT6 and 5-HT2A receptors, and as inhibitors of norepinephrine reuptake. Thus, e.g., II was prepared in multi-step synthesis via cyclization of Me [2-[4-amino-3-[(phenylsulfonyl)methyl]phenyl]ethyl]methylcarbamate (preparation given) followed by deprotection. I showed a high degree of affinity for the 5-HT6 receptor, e.g., II demonstrated Ki value of 5.2 nM for 5-HT6 binding affinity. As modulators of the 5-HT6 and 5-HT2A receptors and inhibitors of norepinephrine reuptake, I are useful in the treatment of disorders related to or associated with the 5-HT receptors or with norepinephrine reuptake inhibition.

L43 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1338085 CAPLUS Full-text

DOCUMENT NUMBER: 146:81756

TITLE: Novel tetracyclic tetrahydrofuran derivatives containing a cyclic amine side chain and their preparation, pharmaceutical compositions and dopamine and serotonin receptor binding affinity

INVENTOR(S): Cid-Nunez, Jose Maria; Trabanco-Suarez, Andres

Avelino

PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.

SOURCE: PCT Int. Appl., 133pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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20060616 WO 2006134163	A2	20061221	WO 2006-EP63273	
WO 2006134163	A3	20070412		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW,				

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 VC, VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
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 AU 2006259020 A1 20061221 AU 2006-259020
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 20060616 EP 1896456 A2 20080312 EP 2006-777340
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 TR, AL, BA, HR, MK, YU
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 20060616 MX 200716247 A 20080310 MX 2007-16247
 20071214 IN 2007DN09744 A 20080620 IN 2007-DN9744
 20071217 US 20080262076 A1 20081023 US 2007-917840
 20071217 KR 2008021793 A 20080307 KR 2008-701391
 20080117 CN 101228154 A 20080723 CN 2006-80026917
 20080123 PRIORITY APPLN. INFO.: EP 2005-105398 A
 20050617 WO 2006-EP63273 W
 20060616
 OTHER SOURCE(S): MARPAT 146:81756
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB This invention concerns novel substituted tetracyclic THF derivs.
 containing a cyclic amine side chain with binding affinities
 towards dopamine receptors, in particular dopamine D2 receptors,
 towards serotonin receptors, in particular 5-HT2A and 5-HT2C
 receptors, and pharmaceutical compns. comprising the compds.
 according to the invention, the use thereof as a medicine, in
 particular for the prevention and/or treatment of a range of

psychiatric and neurol. disorders, in particular certain psychotic, cardiovascular and gastroduodenal disorders and processes for their production. The compds. according to the invention can be represented by general formula I and comprises also a pharmaceutically acceptable acid or base addition salt thereof, an N-oxide form thereof or a quaternary ammonium salt thereof. Compds. of formula I wherein m and n are independently 0, 1, 2, 3, and 4; R1 and R2 are independently halo, CN, OH, carboxyl, NO2, amino, (mono/di)alkylamino, etc. A is (un)substituted cyclic amine; X is (un)substituted CH2, O, S, SO, SO2, NH and derivs.; and their pharmaceutically acceptable acid and base addition salts, N-oxides, and quaternary ammonium salts thereof, are claimed. Compound II was prepared by amination of [2R-(2a,3aa,12b)]-11-fluoro-3,3a,8,12b-tetrahydro-2H-dibenzo[3,4:6,7]cyclohepta[1,2-b]furan-2-methanol 4-methylbenzenesulfonate with 3-pyrrolidinol. All the invention compds. were evaluated for their dopamine D2L and serotonin 5-HT2A and 5-HT2C receptor binding affinities. From the assay, it was determined that compound II exhibited pIC50 values of 8.13 against D2L, 9.43 against 5-HT2C, 9.16 against 5-HT2A, and 6.32 against NET.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:605280 CAPLUS Full-text
 DOCUMENT NUMBER: 145:83221
 TITLE: Preparation of bridged arylpiperidines as nk1 antagonists
 INVENTOR(S): Xiao, Dong; Palani, Anandan; Wang, Cheng; Tsui, Hon-Chung; Huang, Xianhai; Shah, Sapna S.; Rao, Ashwin U.; Chen, Xiao; Paliwal, Sunil; Shih, Neng-Yang
 PATENT ASSIGNEE(S): Schering Corporation, USA
 SOURCE: PCT Int. Appl., 202 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006065654	A1	20060622	WO 2005-US44647	
20051207				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,			

MW, MX,
 SD, SE,
 UZ, VC,
 VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE,
 BF, BJ,
 BW, GH,
 AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 US 20060258665 A1 20061116 US 2005-291363
 20051201
 US 7354922 B2 20080408
 CA 2591079 A1 20060622 CA 2005-2591079
 20051207
 EP 1828188 A1 20070905 EP 2005-849677
 20051207
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK,
 TR, AL,
 BA, HR, MK, YU
 JP 2008523144 T 20080703 JP 2007-546775
 20051207
 MX 200707152 A 20070814 MX 2007-7152
 20070614
 CN 101115753 A 20080130 CN 2005-80048054
 20070813
 PRIORITY APPLN. INFO.: US 2004-635971P P
 20041214
 WO 2005-US44647 W
 20051207
 OTHER SOURCE(S): MARPAT 145:83221
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. I [Arl-2 independently = (un)substituted aryl or heteroaryl; X1 = O, NH, N-alkyl, N-haloalkyl, etc.; X2 = O, CH2, C(alkyl)2, NH, N-alkyl, etc.; X3 = CO, CH2, C(alkyl)2, C(=N-alkyl), etc.; X4 = NH, N-alkyl, CH2, etc.; with provision that when X3 = (un)substituted C, at least one of X2 and X4 also equal (un)substituted C; n = 0-4; R1 = H, OH, (un)substituted alkyl, etc.; R2-5 independently = H, haloalkyl, cycloalkyl, etc.; further provisions allow for when X2 = N the substituent on N may together with R1 form a (un)substituted ring], and their pharmaceutically acceptable salts, were prepared and disclosed as useful in treating diseases or conditions mediated by NK1 receptors, for

example various physiol. disorders, symptoms or diseases, including emesis, depression, anxiety and cough. Thus, e.g., II was prepared in a multistep synthesis from III. Especially preferred compds. of the invention have Ki values of 0.05 nM to about 1 nM for the NK1 receptor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:1176480 CAPLUS Full-text
 DOCUMENT NUMBER: 143:440426
 TITLE: Substituted morpholine compounds for the treatment of

central nervous system disorders, their preparation and pharmaceutical compositions
 INVENTOR(S): Barta, Nancy S.; Glase, Shelly Ann; Gray, David L.; Reichard, Gregory A.; Simons, Lloyd J.; Xu, Weijan

PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
 SOURCE: U.S. Pat. Appl. Publ., 85 pp.
 CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050245519	A1	20051103	US 2005-119210	
20050429				
AU 2005238296	A1	20051110	AU 2005-238296	
20050419				
CA 2564994	A1	20051110	CA 2005-2564994	
20050419				
WO 2005105763	A1	20051110	WO 2005-IB1158	
20050419				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				

DE, DK, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 PL, PT, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL,
 GW, ML, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 MR, NE, SN, TD, TG
 EP 1745029 A1 20070124 EP 2005-733459
 20050419
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
 HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR,
 AL, BA, HR, LV, MK, YU
 CN 1950348 A 20070418 CN 2005-80013776
 20050419
 BR 2005010453 A 20071030 BR 2005-10453
 20050419
 JP 2007535530 T 20071206 JP 2007-510153
 20050419
 JP 4185154 B2 20081126
 NL 1028924 A1 20051101 NL 2005-1028924
 20050429
 NL 1028924 C2 20060427
 IN 2006DN05782 A 20070803 IN 2006-DN5782
 20061005
 MX 2006012505 A 20061215 MX 2006-12505
 20061027
 KR 2007006881 A 20070111 KR 2006-722767
 20061030
 NO 2006005456 A 20070104 NO 2006-5456
 20061127
 JP 2008019267 A 20080131 JP 2007-233201
 20070907
 PRIORITY APPLN. INFO.: US 2004-567244P P
 20040430 JP 2007-510153 A3
 20050419 WO 2005-IB1158 W
 20050419
 OTHER SOURCE(S): CASREACT 143:440426; MARPAT 143:440426
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB The invention relates to compds. of the formula I, which can be
 used in the treatment of central nervous system disorders. In
 compds. I, A is O or S; X is C1-10 alkyl, C2-8 alkenyl, aryl,
 heterocyclyl, C1-6 alkoxy, etc., with each group optionally
 substituted; and R1 - R5 are independently selected from H, OH,
 halo, C1-6 alkyl, aryl, C3-8 cycloalkyl, C2-6 alkenyl, C1-6
 alkoxy, aryloxy, heterocyclyl, etc.; including pharmaceutically
 acceptable salts, enantiomers and diastereomers. The invention

also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of central nervous system disorders. Ring opening of (R,R)-phenylglycidol with 1-naphthol followed by silylation of the primary alc., mesylation of the secondary alc., and desilylation gave mesylate II, which underwent ring closure to the epoxide, ring opening with ammonium hydroxide and amidation with chloroacetyl chloride, resulting in the formation of amide III. Compound III was converted to the morpholine by intramol. cyclization and Red-Al reduction to give morpholine IV. Several compds., e.g., IV, express high inhibition of human norepinephrine transporter (hNET) and human serotonin transporter (hSERT).

L43 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:828046 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 123:306370

ORIGINAL REFERENCE NO.: 123:54623a,54626a

TITLE: The pharmacology of SCH 50911: a novel, orally-active

GABA-B receptor antagonist

AUTHOR(S): Bolser, Donald C.; Blythin, David J.; Chapman, Richard

W.; Egan, Robert W.; Hey, John A.; Rizzo,

Charles;

Kuo, Shen-Chun; kreutner, William

CORPORATE SOURCE: Schering-Plough Res. Inst., Kenilworth, NJ, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics

(1995), 274(3), 1393-8

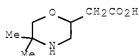
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



HCl

I

AB Expts. were conducted to characterize the pharmacol. of SCH 50911 ((+)-5,5-dimethyl-2-morpholineacetic acid hydrochloride, I), a structurally novel GABA-B receptor antagonist. Although more potent GABA-B antagonists have been reported, in this study SCH 50911 was compared with CGP 35348, a moderately potent and selective GABA-B antagonist with acceptable in vivo activity. SCH 50911 was more potent to inhibit the binding of GABA to the GABA-B receptor in rat brain (IC50 = 1.1 μ M) than CGP 35348 (IC50 = 62 μ M). SCH 50911 had no binding affinity for GABA-A, histamine H1,

histamine H3, dopamine D1, dopamine D2, serotonin 5-HT2, or muscarinic m1, m2, or m4 receptors. However, SCH 50911 (IC50 = 2.2 μ M) was active in a nonspecific muscarinic receptor binding assay, but was devoid of muscarinic agonist or antagonist activity in the isolated guinea pig ileum. SCH 50911 blocked inhibitory responses to baclofen of the guinea pig trachea in a competitive manner ($pa_2 = 5.8 \pm 0.004$). CGP 35348 was 19-fold less potent in this assay ($pa_2 = 4.6 \pm 0.15$). In vivo, SCH 50911 (ED50 = 2.9 mg kg⁻¹, s.c.) and CGP 35348 (ED50 = 5.8 mg kg⁻¹, s.c.) blocked the antitussive effects of baclofen in the guinea pig. In the cat, both SCH 50911 (10 mg kg⁻¹, i.v.) and CGP 35348 (10 mg kg⁻¹, i.v.) shifted the antitussive dose response relationship for baclofen to the right. Baclofen-induced respiratory depression was blocked by s.c. (ED50 = 0.63 mg kg⁻¹), i.p. (ED50 = 1.9 mg kg⁻¹), or oral (ED50 = 3 mg kg⁻¹) administration of SCH 50911. CGP 35348 also blocked the respiratory depressant effect of baclofen but was 3-9 fold less potent than SCH 50911 by these routes of administration. SCH 50911 (50 μ g, i.c.v.) completely blocked respiratory depression by baclofen indicating activity at GABA-B receptors in the CNS. The (-) enantiomer of SCH 50911 was inactive as a GABA-B antagonist. SCH 50911 is a selective, competitive, and orally active GABA-B receptor antagonist. Both central and peripheral GABA-B receptors are blocked by SCH 50911 and this antagonist is more potent than CGP 35348.

L43 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:83609 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 116:83609

ORIGINAL REFERENCE NO.: 116:14239a,14242a

TITLE: Centrally acting α 1-adrenoceptor agonists based

on hexahydronaphth[2,3-b]-1,4-oxazines and octahydrobenzo[g]quinolines

AUTHOR(S): Nozulak, Joachim; Vigouret, Jean M.; Jaton, Anne L.;

Hofmann, Alfred; Dravid, Anant R.; Weber, Hans

P.;

Kalkman, Hans O.; Walkinshaw, Malcolm D.

CORPORATE SOURCE:

Sandoz Pharma Ltd., Basel, CH-4002, Switz.

SOURCE:

Journal of Medicinal Chemistry (1992), 35(3),

480-9

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE:

Journal

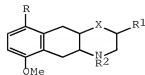
LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 116:83609

GI



I

AB Centrally acting α_1 -agonists may be of therapeutic value in dementias and other CNS disorders characterized by symptoms of noradrenergic insufficiency. Therefore, on the basis of known peripherally acting α_1 -agonists two new groups of centrally acting α_1 -agonists with improved lipophilicity, the hexahydronaphth[2,3-b]-1,4-oxazines I (R = SMe, SEt, NO₂, Cl, R₁ = H, Me, Et, R₂ = Me, Et, X = O) and the octahydrobenzo[gl]quinolines I (R = SMe, SEt, R₁ = H, R₂ = Me, X = CH₂) were prepared. The N-methylated derivs. I (R = SMe, R₁ = H, R₂ = Me, X = O) (II) and I (R = SMe, R₁ = H, R₂ = Me, X = CH₂) demonstrate potent, direct agonistic activity at postjunctional α_1 -receptors. Ring substituent alterations change the potency on the rabbit ear artery by over 3 orders of magnitude (pD₂ = 5.35-8.40). The efficacy of these compds. varies from 42 to 110%. Those α_1 -agonists which were selective in the pithed rat increase vigilance in rats. Compound II was found to be a centrally acting α_1 -agonist with good tolerability in different animal species and in healthy volunteers. Furthermore, II selectively stimulates the breakdown of phosphatidylinositol in rat cerebral cortex slices. In vivo, the compound reverses behavior deficits in animals which received noradrenergic lesions following DDC or DSP₄ treatment. Oxazine II and its close derivs. are by far more lipophilic than commonly known α_1 -agonists.

=> s 141 and (py<2003 or ay<2003 or pry<2003)
 22983269 PY<2003
 4503698 AY<2003
 3972562 PRY<2003

L44 27 L41 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d 144 ibib abs 20-27

L44 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:83609 CAPLUS Full-text

DOCUMENT NUMBER: 116:83609

ORIGINAL REFERENCE NO.: 116:14239a,14242a

TITLE: Centrally acting α_1 -adrenoceptor agonists based

on hexahydronaphth[2,3-b]-1,4-oxazines and octahydrobenzo[gl]quinolines

AUTHOR(S): Nozulak, Joachim; Vigouret, Jean M.; Jaton, Anne L.;

Hofmann, Alfred; Dravid, Anant R.; Weber, Hans

P.;

Kalkman, Hans O.; Walkinshaw, Malcolm D.

CORPORATE SOURCE: Sandoz Pharma Ltd., Basel, CH-4002, Switz.

SOURCE: Journal of Medicinal Chemistry (1992), 35(3), 480-9

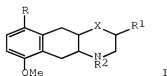
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S):
GI

CASREACT 116:83609



AB Centrally acting α_1 -agonists may be of therapeutic value in dementias and other CNS disorders characterized by symptoms of noradrenergic insufficiency. Therefore, on the basis of known peripherally acting α_1 -agonists two new groups of centrally acting α_1 -agonists with improved lipophilicity, the hexahydronaphth[2,3-b]-1,4-oxazines I (R = SMe, SEt, NO₂, Cl, R₁ = H, Me, Et, R₂ = Me, Et, X = O) and the octahydrobenzo[g]quinolines I (R = SMe, SEt, R₁ = H, R₂ = Me, X = CH₂) were prepared. The N-methylated derivs. I (R = SMe, R₁ = H, R₂ = Me, X = O) (II) and I (R = SMe, R₁ = H, R₂ = Me, X = CH₂) demonstrate potent, direct agonistic activity at postjunctional α_1 -receptors. Ring substituent alterations change the potency on the rabbit ear artery by over 3 orders of magnitude (pD₂ = 5.35-8.40). The efficacy of these compds. varies from 42 to 110%. Those α_1 -agonists which were selective in the pithed rat increase vigilance in rats. Compound II was found to be a centrally acting α_1 -agonist with good tolerability in different animal species and in healthy volunteers. Furthermore, II selectively stimulates the breakdown of phosphatidylinositol in rat cerebral cortex slices. In vivo, the compound reverses behavior deficits in animals which received noradrenergic lesions following DDC or DSP4 treatment. Oxazine II and its close derivs. are by far more lipophilic than commonly known α_1 -agonists.

L44 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1991:449558 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 115:49558

ORIGINAL REFERENCE NO.: 115:8605a,8608a

TITLE: Synthesis and biological activity of some new
2- and

4-(4-aryl-5-mercapto-4H-1,2,4-triazol-3-ylmethyl)-6-

chlorobenzoxazin-3-ones
AUTHOR(S): Sastry, C. V. Reddy; Rao, K. Srinivasa;
Rastogi, K.;

Jain, M. L.
CORPORATE SOURCE: Chem. Div., Indian Drugs and Pharmaceuticals
Ltd.,

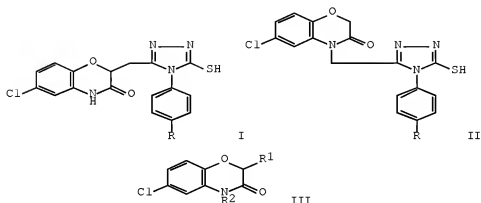
Hyderabad, 500 037, India

SOURCE: Indian Journal of Chemistry, Section B:
Organic

Chemistry Including Medicinal Chemistry (1991

DOCUMENT TYPE:
LANGUAGE:
OTHER SOURCE(S):
GI

), 30B(4), 450-2
CODEN: IJSBDB; ISSN: 0376-4699
Journal
English
CASREACT 115:49558

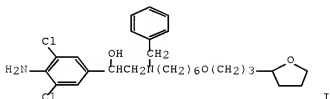


AB Title compds. I and II (R = H, Br, Cl, F) were prepared starting from benzoxazinyllacetates III (R1 = CH2CO2Me, R2 = H; R1 = H, R2 = CH2CO2Et) resp. in 3 steps involving reaction with N2H4 to give the hydrazides, reaction with 4-RC6H4NCS (R = H, Br, Cl, F) to give thiosemicarbazides and intramol. cyclization in refluxing 2 N NaOH solution I, II and thiosemicarbazides III [R1 = CH2CONHNHC(S)NHC6H4R-4, R2 = H; R1 = H, R2 = CH2CONHNHC(S)NHC6H4R-4] were tested for antiinflammatory activity in rats, and β -adrenergic blocking activity in guinea pigs. III [R1 = CH2CONHNHC(S)NHC6H4R-4, R2 = H] showed moderate antiinflammatory activity. III (R1 = CH2CONHNHC(S)NHC6H4F-4) showed a low order of antifungal activity in vitro against some fungi. I and II showed no antiinflammatory activity. None showed any noteworthy β -adrenergic activity.

L44 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:185280 CAPLUS Full-text
DOCUMENT NUMBER: 114:185280
ORIGINAL REFERENCE NO.: 114:31287a,31290a
TITLE: Preparation of phenethanolamine compounds
INVENTOR(S): Lunts, Lawrence Henry Charles; Judkins, Brian
David
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK
SOURCE: Brit. UK Pat. Appl., 35 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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GB 2230775	A	19901031	GB 1989-9274	
19890424 <--				
PRIORITY APPLN. INFO.:			GB 1989-9274	
19890424 <--				
OTHER SOURCE(S):		CASREACT 114:185280; MARPAT 114:185280		
GI				



AB WCH(OH)CH₂NHCR₁R₂XCH₂OCH₂YQ [R₁, R₂ = H, C1-3 alkyl and R₁ + R₂ ≤ 4 C atoms; W = (substituted) Ph; X = bond, C1-7 alkylene, C2-7 alkenylene or alkynylene; Y = bond, C1-6 alkylene, C2-6 alkenylene or alkynylene, and X + Y ≤ 10 C atoms; Q = (substituted) 5-8-membered heterocycle containing one or more of O, S, N atoms], useful as β₂-adrenoreceptor stimulants (no data), were prepared. For example 2-[3-[(6-bromohexyl)oxy]propyl]tetrahydrofuran was subjected to amination by PhCH₂NH₂, N-alkylation by 1-(4-amino-3,5-dichlorophenyl)-2-bromoethanone, and NaBH₄ reduction to give I, which was hydroenolized over 10% Pd/C to give the corresponding title compound.

L44 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1991:143298 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 114:143298

ORIGINAL REFERENCE NO.: 114:24317a, 24320a

TITLE: Novel benzamides as selective and potent gastric

prokinetic agents. 1. Synthesis and structure-activity relationships of N-[(2-morpholinyl)alkyl]benzamides

AUTHOR(S): Kato, Shiro; Morie, Toshiya; Hino, Katsuhiko; Kon,

Tatsuya; Naruto, Shunsuke; Yoshida, Naoyuki;

Karasawa,

Tadahiko; Matsumoto, Junichi

CORPORATE SOURCE: 564,

Res. Lab., Dainippon Pharm. Co., Ltd., Suita, Japan

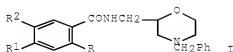
SOURCE: Journal of Medicinal Chemistry (1990),
33(5), 1406-13
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 114:143298

GI



AB In order to obtain more potent and selective gastric prokinetic agents than metoclopramide a new series of 36 N-[(2-morpholinyl)alkyl]benzamides, e.g., I (R = OMe, OEt, OH, Cl; R1 = NH2, NMe2, NEt2, NHAc; R2 = H, Br, Cl, NO2, SO2NH2) were synthesized and their gastric prokinetic activity was evaluated by determining effects on the gastric emptying of phenol red semisolid meal and of resin pellets solid meal in rats and mice. The morpholinyl moiety was newly designed after consideration of the side-chain structure of cisapride and produced the desired activity when coupled with the 4-amino-5-chloro-2-methoxybenzoyl group of both metoclopramide and cisapride. Modification of the substituents of the benzoyl group markedly influenced the activity. In particular, I (R = OMe, R1 = NH2, R2 = Cl), and its 4-(dimethylamino) and 2-ethoxy analogs showed potent and selective gastric prokinetic activity along with a weak dopamine D2 receptor antagonistic activity.

L44 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1990:35775 CAPLUS Full-text

DOCUMENT NUMBER: 112:35775

ORIGINAL REFERENCE NO.: 112:6189a,6192a

TITLE: Synthesis, physicochemical properties and biological

studies of some substituted
2-alkoxy-4-methylmorpholines

AUTHOR(S): Rekka, Eleni; Kourounakis, Panos

CORPORATE SOURCE: Dep. Pharm., Univ. Thessaloniki, Thessaloniki, 540 06,

Greece

SOURCE: European Journal of Medicinal Chemistry (1989), 24(2), 179-84

CODEN: EJMCAS; ISSN: 0223-5234

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 112:35775

GI



AB The title compds. have some structural characteristics of the piperidine-type analgesics and central sympathomimetics. The synthesis of some substituted 2-hydroxy- and 2-alkoxy-4-methylmorpholines, e.g., I (R = H, CH₂CH:CH₂, CH₂C.tplbond.CH, CH₂CHMe₂, (CH₂)nMe, CH₂Ph, CH₂CH₂Ph; n = 2, 3, 7, 15), is presented and studied in terms of electronic and steric effects. Their log P and pKa values were determined and are explained in terms of structural, stereochem., and electronic effects. Acute toxicity and, for some selected cases, antinociceptive and central sympathomimetic activities were evaluated in a preliminary study of biol. properties.

L44 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1989:574109 CAPLUS Full-text
 DOCUMENT NUMBER: 111:174109
 ORIGINAL REFERENCE NO.: 111:29011a,29014a
 TITLE: Benzoxazine derivatives as serotonin antagonists, their preparation and

formulations

containing them
 INVENTOR(S): Tahara, Tetsuya; Kawakita, Takeshi; Yasumoto, Mitsuyoshi; Fukuda, Takemi

PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 21 pp.
 CODEN: EPXXDW

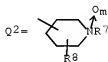
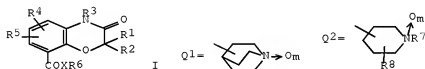
DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
19881021	A2	19890426	EP 1988-309930	
EP 313393	A3	19910206		
EP 313393	B1	19940316		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
JP 01207290	A	19890821	JP 1988-5415	
19880113	C	19920623	CA 1988-580662	
CA 1304082				
19881019	A	19900130	JP 1988-266878	
JP 02028182				
19881021	B	19931015		
JP 05073752	T	19940415	AT 1988-309930	
AT 102943				
19881021				

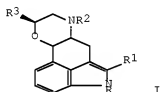
ES 2061684	T3	19941216	ES 1988-309930
19881021 <--			
US 4892872	A	19900109	US 1988-261067
19881024 <--			
PRIORITY APPLN. INFO.:			JP 1987-267953 A
19871022 <--			JP 1987-331259 A
19871225 <--			JP 1988-5415 A
19880113 <--			EP 1988-309930 A
19881021 <--			
OTHER SOURCE(S):	CASREACT 111:174109; MARPAT 111:174109		
GI			



AB The title compds. I [R1, R2 = H, alkyl; R3 = H, alkyl, (substituted) phenylalkyl; R4, R5 = H, halo, alkyl, alkoxy, amino, acylamino, etc.; X = O, NH; R6 = Q1, Q2, etc.; m = 0 or 1; R7 = alkyl, (substituted) phenylalkyl, phenoxyalkyl, etc.; R8 = H, alkoxy], useful as serotonin receptor antagonists, were prepared. A mixture of 3-aminoquinuclidine, N-methylmorpholine, and 6-chloro-3,4-dihydro-4-methyl-3-oxo-2H-1,4-benzoxazine-8-carboxylic acid chloride in CHCl₃ was stirred for 2 h to give, after workup and acidification, 6-chloro-3,4-dihydro-4-methyl-3-oxo-N-(3-quinuclidinyl)-2H-1,4-benzoxazine-8-carboxamide HCl salt (II). II exhibited a MED of 0.5 µg/kg against the von Bezold-Jarish reflex caused by serotonin in rats. Tablets containing II 10, lactose 30, starch 19.8, cellulose 28, talc 2, and Mg stearate 0.2 mg were prepared.

L44 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1984:175119 CAPLUS Full-text
 DOCUMENT NUMBER: 100:175119
 ORIGINAL REFERENCE NO.: 100:26649a,26652a
 TITLE: 9-Oxalysergic acid derivatives
 INVENTOR(S): Nedelec, Lucien; Pierdet, Andre; Fauveau, Patrick
 PATENT ASSIGNEE(S): Roussel-UCLAF, Fr.
 SOURCE: Eur. Pat. Appl., 44 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 94305	A1	19831116	EP 1983-400908	
19830505 <--				
EP 94305	B1	19880113		
R: AT, BE, CH, DE, GB, IT, LI, LU, NL, SE				
FR 2526797	A1	19831118	FR 1982-8249	
19820512 <--				
FR 2526797	B1	19841228		
AT 31929	T	19880115	AT 1983-400908	
19830505 <--				
US 4493836	A	19850115	US 1983-493355	
19830510 <--				
CA 1209573	A1	19860812	CA 1983-427905	
19830511 <--				
JP 59025395	A	19840209	JP 1983-81858	
19830512 <--				
JP 05013955	B	19930223		
PRIORITY APPLN. INFO.:			FR 1982-8249	A
19820512 <--			EP 1983-400908	A
19830505 <--				
OTHER SOURCE(S):	CASREACT 100:175119; MARPAT 100:175119			
GI				



AB Title compds. I (R = H, alkyl, R1 = H, Cl, Br, R2 = H, alkyl, aralkyl, cycloalkylalkyl; R3 = HOCH2, alkylthiomethyl, CH2CN, CO2H, alkoxy carbonyl, amino) were prepared as vasodilators, antihypertensives, dopaminergic agonists, and prolactin secretion inhibitors. Thus, Me (6a-RS)-(6aa,9β,10aβ)-4,5,5a,6,6a,8,9,10a-octahydro-7-methyl-4-benzyl-7H-indolo[3,4-g,h](1,4)benzoxazine-9β-carboxylate (II) was debenzylated by hydrogenolysis followed by MnO2 oxidation to give Me (6a-RS)-(6aa,9β,10aβ)-4,6,6a,8,9,10a-hexahydro-7-methyl-7H-indolo[3,4-g,h](1,4)-benzoxazine-9-carboxylate (III). II was prepared in 5 steps from (4-RS)-trans-4-amino-1-benzoyl-1,2,2a,3,4,5-hexahydrobenz[c,d]indol-5-ol. At 1 mg/kg III reduced the blood pressure of rats.

L44 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1978:68943 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 88:68943
 ORIGINAL REFERENCE NO.: 88:10815a,10818a
 TITLE: Effects of 3,4-dihydro-1H-1,4-oxazino[4,3,-a]

indoles,

potential antidepressants, on biogenic amine

uptake

mechanisms and related activities

AUTHOR(S) :

Lippmann, W.; Pugsley, T. A.

CORPORATE SOURCE:
Montreal.

Biochem. Pharmacol. Dep., Averst Res. Lab.,

.....

OC, Can.

so

Archives Internationales de Pharmacodynamie et

Therapie (1977), 227(2), 324-42

CODEN: AIPTAK; ISSN: 0003-9780

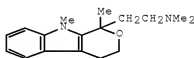
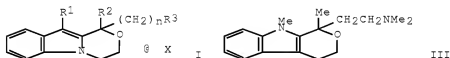
DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI



AB 3,4-Dihydro-1H-1,4-oxazino[4,3-a]indoles (I) were examined for their ability to inhibit norepinephrine (NE) [51-41-2] and serotonin (5-HT) [50-67-9] neuronal membrane uptake mechanisms. Various related activities of the most potent member of this series 3,4-dihydro-1,10-dimethyl-1-(3-methylaminopropyl)-1H-1,4-oxazino[4,3-a]indole-HCl (I, R1 = R2 = Me, R3 = NMe, n = 3, x = HCl) (II) [56209-69-9] were determined and compared to those of a structurally-related tetrahydropyrano[3,4-b]indole, III [42820-0-0], and the tricyclic antidepressants desimipramine (DMI), imipramine (IM) and amitriptyline (AT). II was greater, or generally equivalent, in activity to III, IM, and AT in blocking NE uptake mechanisms, antagonizing reserpine-induced effects, and potentiating the behavioral effects of L-DOPA. II, unlike these compds. was not appreciably effective as a 5-HT uptake inhibitor or central 5-HT potentiator, thus resembling DMI. Neither II nor III exhibited in vivo monoamine oxidase inhibition, and in contrast to DMI, IM, and AT, did not exhibit appreciable antiacetylcholine effects. Both compds. enhanced central dopaminergic activity. Thus II, like DMI, is a relatively selective blocker of neuronal NE uptake and III, like IM and AT, blocks both NE and 5-HT uptake mechanisms, actions considered relevant to potential clin. antidepressant activity.

=> d 144 ibib abs 10-19

L44 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:

2002:2433 CAPLUS Full-text

DOCUMENT NUMBER:

136:194560

TITLE: GABAB receptor inhibition causes locomotor stimulation
in mice

AUTHOR(S): Colombo, Giancarlo; Melis, Samuele; Brunetti, Giuliana; Serra, Salvatore; Vacca, Giovanni; Carai, Mauro A. M.; Gessa, Gian Luigi

CORPORATE SOURCE: "Bernard B. Brodie" Department of Neuroscience,
University of Cagliari, C.N.R. Institute of Neurogenetics and Neuropharmacology,
Monsserrato (CA), I-09042, Italy

SOURCE: European Journal of Pharmacology (2001), 433(1), 101-104
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The present study investigated the effect of the administration of the GABAB receptor antagonists, SCH 50911 [(2S)(+)-5,5-dimethyl-2-morpholine acetic acid], CGP 46381 [(3-aminopropyl)(cyclohexylmethyl)phosphinic acid] and CGP 52432 (3-[[[(3,4-dichlorophenyl)methyl]amino]propyl]diethoxymethyl phosphinic acid), on spontaneous locomotor activity in mice. All drugs were acutely administered at the doses of 10 and 30 mg/kg (i.p.). The dose of 30 mg/kg of all drugs resulted in a significant stimulation of locomotor activity. The locomotor stimulation elicited by SCH 50911 was completely blocked by haloperidol (0.1 mg/kg, i.p.), suggesting that hyperactivity induced by blockade of the GABAB receptor is mediated by enhanced dopamine release. These results suggest the existence of a GABAB receptor-mediated tonic inhibition of dopamine neurons.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:506658 CAPLUS Full-text

DOCUMENT NUMBER: 131:307368

TITLE: Activation of nigral dopamine neurons by the selective GABAB-receptor antagonist SCH 50911

AUTHOR(S): Erhardt, S.; Nissbrandt, H.; Engberg, G.

CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Swed.

SOURCE: Journal of Neural Transmission (1999), 106(5-6), 383-394
CODEN: JNTRF3; ISSN: 0300-9564

PUBLISHER: Springer-Verlag Wien

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous studies have shown that systemic as well as local administration of the GABAB-receptor agonist baclofen is associated with a decrease in firing rate, a regularization of firing rhythm and a decrease in burst firing activity of dopamine

(DA) containing midbrain neurons. In the present electrophysiol. study the authors have utilized the novel, selective and potent GABAB-receptor antagonist SCH 50911 to further analyze the importance of GABAB-receptors for the overall activity of rat nigral DA neurons. SCH 50911 given i.v. (1-64 mg/kg) or locally, by microiontophoretic techniques, was found to increase firing rate and to increase the burst firing activity of DA neurons. The present data suggest that the GABAB-receptor antagonist blocks somatodendritic receptors on nigral DA neurons. This GABA-receptor input appears to be of a tonic nature. It is proposed that the activation of nigral DA neurons may underlie the beneficial effects of GABAB-receptor antagonists in the modulation of cognition and that GABAB-receptor antagonists may be of therapeutic value in the treatment of Parkinson's disease.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:147318 CAPLUS Full-text

DOCUMENT NUMBER: 128:204912

ORIGINAL REFERENCE NO.: 128:40527a,40530a

TITLE: Preparation of disubstituted morpholines, oxazepines

or thiazepines as dopamine D4 receptor antagonists

INVENTOR(S): Axelsson, Oskar; Peters, Dan; Scheel-Kruger, Jorgen;

Ostergaard, Nielsen Elsebet

PATENT ASSIGNEE(S): Neurosearch A/S, Den.; Axelsson, Oskar; Peters, Dan;

Scheel-Kruger, Jorgen; Ostergaard Nielsen,

Elsebet

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

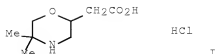
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9807710	A1	19980226	WO 1997-EP4587	
19970822 <--				
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,				

L44 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1998:102440 CAPLUS Full-text
 DOCUMENT NUMBER: 128:239549
 ORIGINAL REFERENCE NO.: 128:47281a,47284a
 TITLE: Binding of 2,4-disubstituted morpholines at
 human D4
 dopamine receptors
 AUTHOR(S): Showell, Graham A.; Emms, Frances; Marwood,
 Rosemarie;
 O'Connor, Desmond; Patel, Smita; Leeson, Paul
 D.
 CORPORATE SOURCE: Neuroscience Research Centre, Merck, Sharp &
 Dohme
 Research Laboratories, Essex, CM20 2QR, UK
 SOURCE: Bioorganic & Medicinal Chemistry (1998),
 6(1), 1-8
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The synthesis of a series of 2,4-disubstituted morpholines is
 described and their affinities at human dopamine receptors
 reported. The orally bioavailable 7-azaindole compound 1 has
 nanomolar affinity at the hD4 receptor with > 1000-fold
 selectivity over the hD2 receptor.
 REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L44 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1995:828046 CAPLUS Full-text
 DOCUMENT NUMBER: 123:306370
 ORIGINAL REFERENCE NO.: 123:54623a,54626a
 TITLE: The pharmacology of SCH 50911: a novel,
 orally-active
 GABA-B receptor antagonist
 AUTHOR(S): Bolser, Donald C.; Blythin, David J.; Chapman,
 Richard
 W.; Egan, Robert W.; Hey, John A.; Rizzo,
 Charles;
 Kuo, Shen-Chun; Kreutner, William
 CORPORATE SOURCE: Schering-Plough Res. Inst., Kenilworth, NJ,
 USA
 SOURCE: Journal of Pharmacology and Experimental
 Therapeutics
 (1995), 274(3), 1393-8
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Expts. were conducted to characterize the pharmacol. of SCH 50911 ((+)-5,5-dimethyl-2-morpholineacetic acid hydrochloride, I), a structurally novel GABA-B receptor antagonist. Although more potent GABA-B antagonists have been reported, in this study SCH 50911 was compared with CGP 35348, a moderately potent and selective GABA-B antagonist with acceptable in vivo activity. SCH 50911 was more potent to inhibit the binding of GABA to the GABA-B receptor in rat brain ($IC_{50} = 1.1 \mu M$) than CGP 35348 ($IC_{50} = 62 \mu M$). SCH 50911 had no binding affinity for GABA-A, histamine H1, histamine H3, dopamine D1, dopamine D2, serotonin 5-HT2, or muscarinic m1, m2, or m4 receptors. However, SCH 50911 ($IC_{50} = 2.2 \mu M$) was active in a nonspecific muscarinic receptor binding assay, but was devoid of muscarinic agonist or antagonist activity in the isolated guinea pig ileum. SCH 50911 blocked inhibitory responses to baclofen of the guinea pig trachea in a competitive manner ($pA_2 = 5.8 \pm 0.004$). CGP 35348 was 19-fold less potent in this assay ($pA_2 = 4.6 \pm 0.15$). In vivo, SCH 50911 ($ED_{50} = 2.9 \text{ mg kg}^{-1}$, s.c.) and CGP 35348 ($ED_{50} = 5.8 \text{ mg kg}^{-1}$, s.c.) blocked the antitussive effects of baclofen in the guinea pig. In the cat, both SCH 50911 (10 mg kg^{-1} , i.v.) and CGP 35348 (10 mg kg^{-1} , i.v.) shifted the antitussive dose response relationship for baclofen to the right. Baclofen-induced respiratory depression was blocked by s.c. ($ED_{50} = 0.63 \text{ mg kg}^{-1}$), i.p. ($ED_{50} = 1.9 \text{ mg kg}^{-1}$), or oral ($ED_{50} = 3 \text{ mg kg}^{-1}$) administration of SCH 50911. CGP 35348 also blocked the respiratory depressant effect of baclofen but was 3-9 fold less potent than SCH 50911 by these routes of administration. SCH 50911 ($50 \mu g$, i.c.v.) completely blocked respiratory depression by baclofen indicating activity at GABA-B receptors in the CNS. The (-) enantiomer of SCH 50911 was inactive as a GABA-B antagonist. SCH 50911 is a selective, competitive, and orally active GABA-B receptor antagonist. Both central and peripheral GABA-B receptors are blocked by SCH 50911 and this antagonist is more potent than CGP 35348.

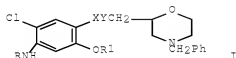
L44 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1995:783361 CAPLUS Full-text
 DOCUMENT NUMBER: 123:339949
 ORIGINAL REFERENCE NO.: 123:61011a,61014a
 TITLE: Synthesis and gastroprokinetic activity of
 N-(4-amino-5-chloro-2-methoxyphenyl)-4-benzyl-

2-

AUTHOR(S): morpholineacetamide and related compounds
 Kato, S.; Morie, T.; Yoshida, N.; Fujiwara,
 I.; Kon,

T.
 CORPORATE SOURCE: Exploratory Research Laboratories, Dainippon
 Pharmaceutical Co Ltd, Osaka, 564, Japan

SOURCE: European Journal of Medicinal Chemistry (1995
, 30(7-8), 609-16
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Benzamide derivs. I (XY = CONH; R = H; R1 = Me, Et) show potent gastroprokinetic activity. To exam. the effect of reversal of the amide linkage, I (XY = NHCO; R = H, acyl, MeSO2; R1 = Me) were prepared and evaluated for gastroprokinetic activity by determining their effects on gastric emptying of a phenol red semisolid meal and a serotonin-4 receptor binding assay. Reversal of the amide bond decreased the activity. A mol. superposition procedure, using computer graphics, suggested that the location of the morpholine ring and N-benzyl group is crucial for activity.

L44 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:772766 CAPLUS [Full-text](#)
DOCUMENT NUMBER: 123:228200
ORIGINAL REFERENCE NO.: 123:40767a,40770a
TITLE: Morpholine derivatives as dopamine receptor
subtype ligands and their preparation,
compositions,
and use
INVENTOR(S): Leeson, Paul David; Showell, Graham Andrew
PATENT ASSIGNEE(S): Merck Sharp and Dohme Ltd., UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

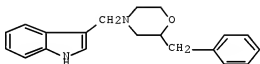
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514690	A1	19950601	WO 1994-GB2557	
19941121 <--				
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,				
GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,				
NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				

RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
 IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
 NE, SN, TD, TG

AU 9510719 A 19950613 AU 1995-10719
 19941121 <--
 AU 680320 B2 19970724
 EP 730593 A1 19960911 EP 1995-901522
 19941121 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL,
 PT, SE
 US 5614518 A 19970325 US 1996-647926
 19960520 <--
 PRIORITY APPLN. INFO.: GB 1993-24018 A
 19931123 <-- WO 1994-GB2557 W
 19941121 <--
 OTHER SOURCE(S): CASREACT 123:228200; MARPAT 123:228200
 GI



I



II

AB A class of substituted morpholine derivs. is disclosed, specifically I [Y = (un)substituted bicyclic heteroarom. ring system containing 1 or 2 N atoms, the ring system comprising a six-membered aromatic or heteroarom. ring fused to a five- or six-membered heteroarom. ring; Z = (un)substituted arylalkyl, aryloxymethyl or arylalkoxymethyl], and their salts and prodrugs. I are ligands for dopamine receptor subtypes, and are therefore useful in the treatment and/or prevention of a variety of disorders of the dopamine system, in particular schizophrenia. For example, condensation of 3-[(dimethylamino)methyl]indole with (R,S)-2-(phenylmethyl)morpholine by heating in refluxing toluene for 16 h gave 92% title compound II. Fourteen examples of I and several salts were prepared, and all were found to have K_i of < 1.5 μ M for displacement of [3H]-spiperone from human dopamine D4 receptors in a binding assay.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L44 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1995:763484 CAPLUS Full-text
 DOCUMENT NUMBER: 123:169510
 ORIGINAL REFERENCE NO.: 123:30259a,30262a
 TITLE: Phenoxyalkylamines, -pyrrolidines and -

piperidines for

diseases

the treatment and prevention of circulatory

and psychosis.

INVENTOR(S):

Fumitoshi; Ito,

Fujimoto, Koichi; Tanaka, Naoki; Asai,

Tomiyoshi; Koike, Hiroyuki

PATENT ASSIGNEE(S):

Sankyo Co., Ltd., Japan

SOURCE:

Eur. Pat. Appl., 218 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

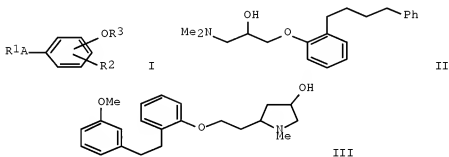
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 600717	A1	19940608	EP 1993-309570	
19931130 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC,				
NL, PT, SE				
CA 2110251	A1	19940531	CA 1993-2110251	
19931129 <--				
NO 9304311	A	19940531	NO 1993-4311	
19931129 <--				
HU 70031	A2	19950928	HU 1993-3376	
19931129 <--				
TW 385302	B	20000321	TW 1993-82110056	
19931129 <--				
FI 9305341	A	19940531	FI 1993-5341	
19931130 <--				
FI 106957	B1	20010515		
AU 9352017	A	19940609	AU 1993-52017	
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AU 666590	B2	19960215		
ZA 9308959	A	19940803	ZA 1993-8959	
19931130 <--				
JP 06306025	A	19941101	JP 1993-299408	
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CN 1102640	A	19950517	CN 1993-121646	
19931130 <--				
CN 1044365	C	19990728		
RU 2105752	C1	19980227	RU 1993-53036	
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IL 107808	A	19980405	IL 1993-107808	
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EP 844000	A1	19980527	EP 1997-114529	
19931130 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT, IE				
CZ 283720	B6	19980617	CZ 1993-2582	
19931130 <--				
JP 06234736	A	19940823	JP 1993-318553	
19931217 <--				
JP 3154884	B2	20010409		
US 5556864	A	19960917	US 1995-369255	

19950105 <--
 FI 9800816 A 19980409 FI 1998-816
 19980409 <--
 FI 106551 B1 20010228
 PRIORITY APPLN. INFO.: JP 1992-320609 A
 19921130 <-- JP 1992-338307 A
 19921218 <-- EP 1993-309570 A3
 19931130 <-- FI 1993-5341 A
 19931130 <-- US 1993-159744 B1
 19931130 <--
 OTHER SOURCE(S): CASREACT 123:169510; MARPAT 123:169510
 GI



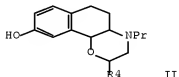
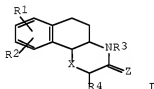
AB Phenoxyalkylamines I [R1 = aryl; R2 = H, alkyl, alkoxy, halo, cyano; R3 = group BNR4R5; R4, R5 = H, alkyl; R4R5 = together with the N form heterocyclic group; B = alkylene, group CH2CH(OR6)CH2; R6 = H, alkanoyl, arylcarbonyl, group DR7; D = single bond, alkylene; R7 = heterocyclic group; A = alkylene] were disclosed as serotonergic S2 and/or dopaminergic D2 antagonists. Claimed example compds. are 3-(dimethylamino)-1-[2-(4-phenylbutyl)phenoxy]-2-propanol (II) and 4-hydroxy-1-methyl-2-[2-[2-(3-methoxyphenyl)ethyl]phenoxy]ethylpyrrolidine (III). I and pharmaceutically acceptable salts and esters thereof are useful for the treatment and prevention of circulatory diseases and psychosis.

L44 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1994:483352 CAPLUS Full-text
 DOCUMENT NUMBER: 121:83352
 ORIGINAL REFERENCE NO.: 121:14985a,14988a
 TITLE: Preparation of naphthoxazines and analogs as dopaminergic agonists
 INVENTOR(S): Peck, James VanOlden; Minasakanian, Gevork

PATENT ASSIGNEE(S): Whitby Research, Inc., USA
 SOURCE: PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324471	A1	19931209	WO 1993-US5305	

19930602 <--
 W: CA, JP
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE
 PRIORITY APPLN. INFO.: US 1992-889940 A
 19920602 <--
 OTHER SOURCE(S): MARPAT 121:83352
 GI



AB Title compds. [I; R1,R2 = H, OH, alkoxy, O2CR5, etc.; R3 = alkyl; R4 = (CH2)nCO2R6, (CH2)nCHRR7; R = (hetero)aryl; R5 = alkyl, aryl; R6 = H, alkyl; R7 = H, alkyl, alkoxy, alkanoyloxy; X = CH2, O, S, NH, etc.; Z = H2, O, S; n = 0-4] were prepared. Thus, trans-1a,2,4,4a,5,6-hexahydro-9-methoxy-4-propylnaphth[1,2-b]-1,4-oxazin-3-one was converted in 3 steps to title compound II (R4 = CH2Ph). (+)-II.HCl (R4 = α -CH2Ph) had pKi of 7.50 and 5.89 for binding at dopamine D2 and D1 receptors, resp.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE

L44 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:38668 CAPLUS [Full-text](#)

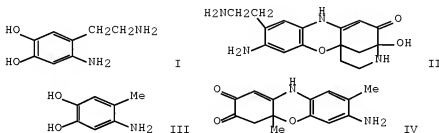
DOCUMENT NUMBER: 118:38668

ORIGINAL REFERENCE NO.: 118:7039a,7042a

TITLE: A new oxidation pathway of the neurotoxin 6-aminodopamine. Isolation and

characterization of a dimer with a tetrahydro[3,4a]iminoethanophenoxazine

AUTHOR(S): ring system
 Napolitano, Alessandra; D'Ischia, Marco;
 Costantini, Claudio; Prota, Giuseppe
 CORPORATE SOURCE: Dep. Org. Biol. Chem., Univ. Naples, Naples,
 I-80134, Italy
 SOURCE: Tetrahedron (1992), 48(39), 8515-22
 CODEN: TETRAB; ISSN: 0040-4020
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Oxidation of the neurotoxin 6-aminodopamine (I) is known to proceed through the o-quinone, which undergoes intramol. cyclization to give 5,6-dihydroxyindole. In a re-examination of the reaction, it was found that at concns. of I higher than $5 + 10^{-3}$ M a quite different course prevails, leading to the formation of the novel 7-amino-8-(2-aminoethyl)-3-hydroxy-2-oxo-2,3,4,10-tetrahydro[3,4a]iminoethanophenoxazine (II). II was formed by aerobic, chemical (persulfate, periodate) or enzymic (tyrosinase, peroxidase/H₂O₂) oxidation of I. Oxidation of the model compound 5-amino-4-methylcatechol (III) proceeded similarly to I, giving tetrahydrophenoxazinedione IV.

=> d 144 ibib abs 1-19

L44 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:100738 CAPLUS Full-text
 DOCUMENT NUMBER: 144:198849
 TITLE: Novel dosage form comprising modified-release
 and immediate-release active ingredients
 INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand,
 Sunil;
 PATENT ASSIGNEE(S): Gupta, Vinod Kumar
 India
 SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part
 of U.S.

DOCUMENT TYPE: Ser. No. 630,446.
 LANGUAGE: CODEN: USXXCO
 FAMILY ACC. NUM. COUNT: 2 Patent
 PATENT INFORMATION: English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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20050519 <--	A1	20060202	US 2005-134633	
20020805 <--	A	20040529	IN 2002-MU697	
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20020805 <--	A	20040529	IN 2002-MU699	
20020805 <--	A	20050204	IN 2003-MU80	
20030122	A	20050204	IN 2003-MU82	
20030122	A1	20040520	US 2003-630446	
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PRIORITY APPLN. INFO.:				
20020805 <--			IN 2002-MU699	A
20020805 <--			IN 2003-MU80	A
20030122			IN 2003-MU82	A
20030122			US 2003-630446	A2
20030729				

AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.

L44 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:586215 CAPLUS Full-text
 DOCUMENT NUMBER: 143:120526
 TITLE: Pharmaceutical compositions based on
 anticholinergics

INVENTOR(S): and additional active ingredients
 Pairret, Michel; Pieper, Michael P.; Meade,
 Christopher
 John Montague; Reichl, Richard; Schmelzer,
 Christel;
 Jung, Birgit
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg,

Germany

SOURCE:

of U.S.

U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part

Ser. No. 824,391.

CODEN: USXXCO

Patent

English

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

19

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US 20050148562	A1	20050707	US 2004-6940	
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DE 10062712	A1	20020620	DE 2000-10062712	
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US 6696042	B2	20040224		

US 20040024007	A1	20040205	US 2003-613783	
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US 20040151770	A1	20040805	US 2004-763894	
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AU 2008202554	A1	20080703	AU 2008-202554	
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20030414	US 2003-419358	A1
20030421	US 2003-613783	A2
20030703	US 2004-763894	A2
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20040210	US 2004-776757	A2
20040211	US 2004-824391	A2
20040414	CA 2001-2436540	A3
20011023 <--	US 2001-40196	B1
20011025 <--	US 2003-395777	A1
20030324	AU 2006-202723	A3

20060626

OTHER SOURCE(S): MARPAT 143:120526

AB A pharmaceutical composition comprising an anticholinergic and at least one addnl. active ingredient selected from among corticosteroids, dopamine agonists, PDE-IV inhibitors, NK1-antagonists, endothelin antagonists, antihistamines, and EGFR-kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Among a number of compds. prepared was N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2- [4-[(3-hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-phenylacetamide. Inhalable powders include a formulation containing tiotropium bromide, budesonide, and lactose.

L44 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:513545 CAPLUS Full-text

DOCUMENT NUMBER: 141:71567

TITLE: Preparation of 2-phenylmorpholines and related compounds as dopamine agonists in the treatment of sexual dysfunction.

INVENTOR(S): Allerton, Charlotte Moria Norfor; Baxter, Andrew

Wong, Douglas; Cook, Andrew Simon; Hepworth, David;

Stephen Kwok-fung

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

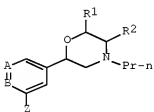
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

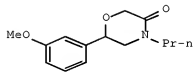
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052372	A1	20040624	WO 2003-IB5683	
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2508262	A1	20040624	CA 2003-2508262	
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US 20040259874	A1	20041223	US 2003-727168	
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US 7323462	B2	20080129		
EP 1572214	A1	20050914	EP 2003-812639	
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BR 2003017102	A	20051025	BR 2003-17102	
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CN 1723023	A	20060118	CN 2003-80105677	
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JP 3889775	B2	20070307		
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IN 2005DN02094	A	20070105	IN 2005-DN2094	
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NO 2005002557	A	20050906	NO 2005-2557	
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MX 2005006151	A	20050826	MX 2005-6151	
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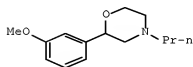
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20050609 <--	JP 2006232857	A	20060907	JP 2006-157609	
20060606 <--	JP 3920908	B2	20070530		
	US 20060235016	A1	20061019	US 2006-425030	
20060619 <--	JP 2007084575	A	20070405	JP 2006-352505	
20061227 <--	PRIORITY APPLN. INFO.:			GB 2002-28787	A
20021210 <--				GB 2003-8460	A
20030411				GB 2003-13606	A
20030612				US 2003-438476P	P
20030107				US 2003-470950P	P
20030515				US 2003-501512P	P
20030908				CN 2003-80105677	A3
20031202				JP 2005-502342	A3
20031202				US 2003-727168	A3
20031202				WO 2003-IB5683	W
20031202				JP 2006-157609	A3
20060606					
OTHER SOURCE(S):	MARPAT 141:71567				
GI					



I



II



III

AB Title compds. I [A = C-X, N; B = C-Y, N; R1 = H, alkyl; R2 = H, alkyl; X = H, OH, CONH2, etc.; Y = H, OH, NH2, etc.; Z = H, OH, F, etc.] their enantiomers and pharmaceutically acceptable salts were

prepared For example, BH3-THF reduction of lactam II, e.g., prepared from 3-methoxybenzaldehyde in 5-steps, afforded 2-phenylmorpholine III in 84% yield. Compds. I expressed EC50 values < 1000 nM with 10-fold selectivity for D3 over D2, e.g., one example of compound I exhibited an EC50 value of 7.6 nM and 1315.8 fold selectivity for D3 over D2. Compds. I are claimed useful for the treatment of sexual dysfunction, e.g., hypoactive sexual activity, orgasmic disorders, erectile dysfunction, etc.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE

L44 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:392318 CAPLUS Full-text
 DOCUMENT NUMBER: 140:400077
 TITLE: Pharmaceutical combinations including either a 5-HT4
 receptor agonist or antagonist or a 5-HT3
 receptor antagonist and a co-agent and their use in
 treating gastrointestinal and abdominal visceral
 disorders
 INVENTOR(S): Billstein, Stephan Anthony; Dumovic, Peter;
 Franco, Nicola; Iwicki, Mark Thomas; Pfannkuche, Hans-
 Jurgen;
 Wilusz, Edward Joseph
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont. of U.S.
 Ser. No. 722,784, abandoned.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040092511	A1	20040513	US 2003-702688	
20031106 <--				
US 20080090878	A1	20080417	US 2007-973404	
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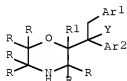
AB The invention discloses a combination of a first agent including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and pharmaceutical compns. and formulations containing the combination. The invention also discloses a method for treating a gastrointestinal and abdominal

visceral disorder by administering the pharmaceutical compns. to a patient. The pharmaceutical compns. may also be employed as laxatives, to prepare a patient for colonoscopy and to regulate and stabilize enterochromaffin cell secretory, pain and motility mechanisms, afferent fiber activity and GI and lower abdominal smooth muscle cells. The dosage is preferably oral and administration is preferably once or twice a day. The preferred first agent is tegaserod.

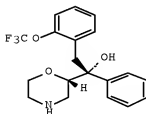
L44 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:182855 CAPLUS Full-text
 DOCUMENT NUMBER: 140:217649
 TITLE: Preparation of aryl and heteroaryl morpholine derivatives as norepinephrine reuptake inhibitors
 INVENTOR(S): Cases-Thomas, Manuel Javier; Haughton, Helen Louise;
 Lamas-Peteira, Carlos; Ouwerkerk-Mahadevan, Sivi;
 Rudyk, Masters, John Joseph; Simmonds, Robin George;
 Helene Catherine Eugenie; Walter, Magnus Wilhelm
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 82 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018441	A1	20040304	WO 2003-US23270	
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 OTHER SOURCE(S): MARPAT 140:217649
 GI



I



II

AB Morpholine derivs. of formula I [R = independently H, alkyl; R1 = H, alkyl; Y = OH, alkoxy; Ar1, Ar2 = (substituted) Ph, (substituted) heteroaryl] are prepared. The compds. are selective inhibitors of the reuptake of norepinephrine. Thus, II.HCl was prepared from (4-benzylmorpholin-2-yl)-phenylmethanone (preparation given) and 2-(trifluoromethoxy)benzyl bromide. The compds. had Ki values less than 500 nM at the norepinephrine transporter in a scintillation proximity assay.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:182714 CAPLUS Full-text
 DOCUMENT NUMBER: 140:235724
 TITLE: Preparation of benzyl morpholine derivatives capable

of selectively inhibiting norepinephrine reuptake

INVENTOR(S): Walter, Magnus Wilhelm; Clark, Barry Peter;

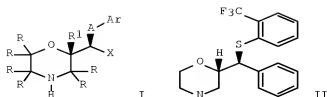
Peter Thaddeus; Haughton, Helen Louise; Rudyk,

Helene

Catherine Eugenie

PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 81 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004017977	A2	20040304	WO 2003-US23269	
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WO 2004017977	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2003269923	A1	20040311	AU 2003-269923	
20030818 <--				
EP 1534291	A2	20050601	EP 2003-751812	
20030818 <--				
EP 1534291	B1	20081112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 413882	T	20081115	AT 2003-751812	
20030818 <--				
US 20060035894	A1	20060216	US 2005-524650	
20050217 <--				
US 7384941	B2	20080610		
PRIORITY APPLN. INFO.:			GB 2002-19690	A
20020823 <--				
20021001 <--			US 2002-415328P	P
20030818			WO 2003-US23269	W
OTHER SOURCE(S):	MARPAT	140:235724		
GI				



AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl group, a cycloalkyl group or cycloalkylmethyl group] and pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared via substitution of (2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (preparation given) with 2-trifluoromethylthiophenol with subsequent debenzoylation. I have been found to exhibit a Ki value less than 500nM at the norepinephrine transporter as determined by scintillation proximity assays. In addition, I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE

FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:41441 CAPLUS Full-text

DOCUMENT NUMBER: 140:93935

TITLE: N-benzyl-3-phenyl-3-heterocyclyl-propionamide compounds as tachykinin/serotonin reuptake inhibitors

INVENTOR(S): Alvaro, Giuseppe; Cardullo, Francesca; D'adamo,

Lucilla; Piga, Elisabetta; Seri, Catia

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005255	A1	20040115	WO 2003-EP7126	

20030702 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI,
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AU 2003281220 A1 20040123 AU 2003-281220
20030702 <--
EP 1517894 A1 20050330 EP 2003-740413
20030702 <--
EP 1517894 B1 20060906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006501182 T 20060112 JP 2004-518695
20030702 <--
AT 338748 T 20060915 AT 2003-740413
20030702 <--
ES 2271606 T3 20070416 ES 2003-740413
20030702 <--
US 20060058348 A1 20060316 US 2005-521159
20050811 <--
PRIORITY APPLN. INFO.: GB 2002-15392 A
20020703 <--
WO 2003-EP7126 W
20030702
OTHER SOURCE(S): MARPAT 140:93935
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB Title compds. I [R = halo, alkyl, CN, alkoxy, etc.; R1 = 5-6-
membered heteroaryl, etc.; R2 = H, alkyl; R3-4 = H, alkyl,
cycloalkyl; R5 = CF3, SOO-2, etc.; L = single or double bond; n =
1-3; m = 0-3] are prepared For instance, 4-[2-Carboxy-1-(4-
fluorophenyl)ethyl]piperidine-1-carboxylic acid tert-Bu ester
(preparation given) is coupled to [3,5-
bis(trifluoromethyl)benzyl]methylaniline and deprotected to give II.
Compds. of the invention have pKi = 10.44 to 7.54 for the NK1
receptor. I are useful in the treatment of conditions mediated by

tachykinins and/or by selective inhibition of serotonin reuptake transporter protein.
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:2708 CAPLUS Full-text
 DOCUMENT NUMBER: 140:53450
 TITLE: Serotonin reuptake inhibitor combination with a GABAB receptor antagonist for the treatment of depression and other disorders
 INVENTOR(S): Mork, Arne; Cremers, Thomas Ivo Franciscus Willigers, Sandra
 PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000326	A1	20031231	WO 2003-DK412	
20030619 <--				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490638	A1	20031231	CA 2003-2490638	
20030619 <--				
CA 2490638	C	20080122		
CA 2579520	A1	20031231	CA 2003-2579520	
20030619 <--				
AU 2003240434	A1	20040106	AU 2003-240434	
20030619 <--				
BR 2003011503	A	20050222	BR 2003-11503	

20030619 <--
 EP 1545552 A1 20050629 EP 2003-729907
 20030619 <--
 EP 1545552 B1 20070328
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1662246 A 20050831 CN 2003-814438
 20030619 <--
 JP 2005533069 T 20051104 JP 2004-514582
 20030619 <--
 AT 357920 T 20070415 AT 2003-729907
 20030619 <--
 ES 2282632 T3 20071016 ES 2003-729907
 20030619 <--
 NZ 536624 A 20080430 NZ 2003-536624
 20030619 <--
 CN 101358379 A 20090204 CN 2008-10215884
 20030619 <--
 ZA 2004009278 A 20060426 ZA 2004-9278
 20041118 <--
 IN 2004CN03184 A 20060303 IN 2004-CN3184
 20041213 <--
 MX 2004012693 A 20050323 MX 2004-12693
 20041215 <--
 NO 2004005552 A 20041220 NO 2004-5552
 20041220 <--
 US 20050288355 A1 20051229 US 2005-516519
 20050725 <--
 PRIORITY APPLN. INFO.: DK 2002-943 A
 20020620 <--
 US 2002-390851P P
 20020620 <--
 CA 2003-2490638 A3
 20030619
 CN 2003-814438 A3
 20030619
 WO 2003-DK412 W

20030619
 AB The invention relates to the use of a compound, which is a
 serotonin reuptake inhibitor, and another compound, which is a
 GABAB receptor antagonist, inverse agonist or partial agonist for
 the preparation of a pharmaceutical composition for the treatment
 of depression, anxiety disorders and other affective disorders,
 such as generalized anxiety disorder, panic anxiety, obsessive
 compulsive disorder, acute stress disorder, post traumatic stress
 disorder and social anxiety disorder, eating disorders such as
 bulimia, anorexia and obesity, phobias, dysthymia, premenstrual
 syndrome, cognitive disorders, impulse control disorders,
 attention deficit hyperactivity disorder, drug abuse or any other
 disorder responsive to serotonin reuptake inhibitors.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

ACCESSION NUMBER: 2002:932584 CAPLUS Full-text
 DOCUMENT NUMBER: 139:17446
 TITLE: SSR240600 [(R)-2-(1-{2-[4-{2-[3,5-bis(trifluoromethyl)phenyl]acetyl}-2-(3,4-dichlorophenyl)-2-morpholinyl]ethyl}-4-piperidinyl)-2-methylpropanamide], a centrally active nonpeptide antagonist of the tachykinin neurokinin 1 receptor:
 II. Neurochemical and behavioral characterization
 AUTHOR(S): Steinberg, Regis; Alonso, Richard; Rouquier, Liliiane; Desvignes, Christophe; Michaud, Jean-Claude; Cudennec, Annie; Jung, Mireille; Simiand, Jacques; Griebel, Guy; Emonds-Alt, Xavier; Le Fur, Gerard; Soubrie, Philippe
 CORPORATE SOURCE: C.N.S. Research Department, Sanofi-Synthelabo Recherche, Montpellier, Fr.
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 303(3), 1180-1188
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB SSR240600 , a new nonpeptide tachykinin neurokinin 1 (NK1) receptor antagonist, was evaluated against the neurochem., electrophysiol., and behavioral effects provoked by direct activation of brain tachykinin NK1 receptors or by stress in guinea pigs. SSR240600 (0.1-10 mg/kg i.p. or p.o.) antagonized the excitatory effect of i.c.v. infusion of [Sar9, Met(02)11]substance P (SP) on the release of acetylcholine in the striatum of anesthetized and awake guinea pigs. This antagonistic action was still observed after repeated administration of SSR240600 (5 days, 10 mg/kg p.o., once a day). SSR240600 (10 mg/kg i.p.) inhibited the phosphorylation of the cAMP response element-binding protein in various brain regions induced by i.c.v. administration of [Sar9, Met(02)11]SP. In slice prepns., neuronal firing of the locus coeruleus (LC) neurons elicited by the application of [Sar9, Met(02)11]SP was suppressed by SSR240600 at 100 nM. Norepinephrine release in the prefrontal cortex, elicited either by an intra-LC application of [Sar9, Met(02)11]SP or by an i.c.v. administration of corticotropin-releasing factor, was reduced by SSR240600 (0.3-1 mg/kg and 1-10 mg/kg i.p., resp.). SSR240600 (1-10 mg/kg i.p.) inhibited vocalizations induced in adult guinea pigs by an i.c.v. administration of the NK1 receptor agonist, GR73632 [D-Ala-[L-Pro9, Me-Leu9]substance P(7-11)]. Furthermore, SSR240600 (1-10 mg/kg i.p.) inhibited distress vocalizations produced in guinea pig pups by maternal separation. SSR240600 also reduced maternal separation-induced increase in the number of neurons displaying

NK1 receptor internalization in the amygdala. Finally, SSR240600 counteracted the increase in body temperature induced by isolation stress. In conclusion, SSR240600 is able to antagonize various NK1 receptor-mediated as well as stress-mediated effects in the guinea pig.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:2433 CAPLUS Full-text

DOCUMENT NUMBER: 136:194560

TITLE: GABAB receptor inhibition causes locomotor stimulation

in mice

AUTHOR(S): Colombo, Giancarlo; Melis, Samuele; Brunetti, Giuliana; Serra, Salvatore; Vacca, Giovanni;

Carai,

Mauro A. M.; Gessa, Gian Luigi

CORPORATE SOURCE: "Bernard B. Brodie" Department of Neuroscience,

University of Cagliari, C.N.R. Institute of Neurogenetics and Neuropharmacology,

Monsserrato (CA),

I-09042, Italy

SOURCE: European Journal of Pharmacology (2001),

433(1), 101-104

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The present study investigated the effect of the administration of the GABAB receptor antagonists, SCH 50911 [(2S)(+)-5,5-dimethyl-2-morpholine acetic acid], CGP 46381 [(3-aminopropyl)(cyclohexylmethyl)phosphinic acid] and CGP 52432 (3-[(3,4-dichlorophenyl)methyl]amino]propyl diethoxymethyl phosphinic acid), on spontaneous locomotor activity in mice. All drugs were acutely administered at the doses of 10 and 30 mg/kg (i.p.). The dose of 30 mg/kg of all drugs resulted in a significant stimulation of locomotor activity. The locomotor stimulation elicited by SCH 50911 was completely blocked by haloperidol (0.1 mg/kg, i.p.), suggesting that hyperactivity induced by blockade of the GABAB receptor is mediated by enhanced dopamine release. These results suggest the existence of a GABAB receptor-mediated tonic inhibition of dopamine neurons.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:506658 CAPLUS Full-text

DOCUMENT NUMBER: 131:307368

TITLE: Activation of nigral dopamine neurons by the selective GABAB-receptor antagonist SCH 50911

AUTHOR(S): Erhardt, S.; Nissbrandt, H.; Engberg, G.

CORPORATE SOURCE: Department of Physiology and Pharmacology,
Karolinska Institute, Stockholm, Swed.

SOURCE: Journal of Neural Transmission (1999),
106(5-6), 383-394
CODEN: JNTRF3; ISSN: 0300-9564

PUBLISHER: Springer-Verlag Wien

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous studies have shown that systemic as well as local
administration of the GABAB-receptor agonist baclofen is
associated with a decrease in firing rate, a regularization of
firing rhythm and a decrease in burst firing activity of dopamine
(DA) containing midbrain neurons. In the present electrophysiol.
study the authors have utilized the novel, selective and potent
GABAB-receptor antagonist SCH 50911 to further analyze the
importance of GABAB-receptors for the overall activity of rat
nigral DA neurons. SCH 50911 given i.v. (1-64 mg/kg) or locally,
by microiontophoretic techniques, was found to increase firing
rate and to increase the burst firing activity of DA neurons. The
present data suggest that the GABAB-receptor antagonist blocks
somatodendritic receptors on nigral DA neurons. This GABA-
receptor input appears to be of a tonic nature. It is proposed
that the activation of nigral DA neurons may underlie the
beneficial effects of GABAB-receptor antagonists in the modulation
of cognition and that GABAB-receptor antagonists may be of
therapeutic value in the treatment of Parkinson's disease.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L44 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:147318 CAPLUS Full-text

DOCUMENT NUMBER: 128:204912

ORIGINAL REFERENCE NO.: 128:40527a,40530a

TITLE: Preparation of disubstituted morpholines,
oxazepines
or thiazepines as dopamine D4 receptor
antagonists

INVENTOR(S): Axelsson, Oskar; Peters, Dan; Scheel-Kruger,
Jorgen;

PATENT ASSIGNEE(S): Ostergaard, Nielsen Elsebet
Neurosearch A/S, Den.; Axelsson, Oskar;
Peters, Dan;
Scheel-Kruger, Jorgen; Ostergaard Nielsen,
Elsebet

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

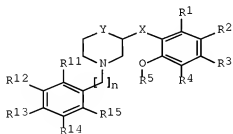
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9807710 A1 19980226 WO 1997-EP4587
 19970822 <--
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU,
 CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
 NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
 UG, US, UZ, VN, YU, ZW
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, ML, MR, NE, SN, TD, TG
 AU 9744553 A 19980306 AU 1997-44553
 19970822 <--
 EP 920423 A1 19990609 EP 1997-942872
 19970822 <--
 EP 920423 B1 20050126
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, FI
 AT 287878 T 20050215 AT 1997-942872
 19970822 <--
 US 6207662 B1 20010327 US 1999-242693
 19990223 <--
 US 6479491 B1 20021112 US 2000-709297
 20001113 <--
 PRIORITY APPLN. INFO.: DK 1996-883 A
 19960823 <--
 WO 1997-EP4587 W
 19970822 <--
 US 1999-242693 A3
 19990223 <--
 OTHER SOURCE(S): MARPAT 128:204912
 GI



I

AB The title compds. [I; R1-R4, R11-R15 = H, alkyl, alkoxy, halo, etc.; R5 = H, alkyl, alkoxyalkyl, phenylalkyl; X = CH2Z, ZCH2, NHCO, CONH, CH:CH (wherein Z = O, S, CH2, NH); Y = O, CH2W, WCH2

(wherein W = O, S); n = 0-2] and their pharmaceutically acceptable acid addition salts and enantiomers, useful in the treatment of psychotic disorders such as schizophrenia, were prepared. Thus, reaction of 4-(4-chlorobenzyl)-2-chloromethylmorpholine with 4-chloro-2-methoxyphenol in the presence of EtOK and 18-crown-6 in PhMe afforded 57% I [R1, R2, R4, R11, R12, R14, R15 = H; R3 = R13 = Cl; R5 = Me; X = CH2O; Y = O; n = 1] which showed IC50 of 0.004 µM against dopamine receptor D4 binding.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:102440 CAPLUS Full-text

DOCUMENT NUMBER: 128:239549

ORIGINAL REFERENCE NO.: 128:47281a, 47284a

TITLE: Binding of 2,4-disubstituted morpholines at human D4

dopamine receptors

AUTHOR(S): Showell, Graham A.; Emms, Frances; Marwood, Rosemarie;

O'Connor, Desmond; Patel, Smita; Leeson, Paul

D.

CORPORATE SOURCE: Neuroscience Research Centre, Merck, Sharp & Dohme

Research Laboratories, Essex, CM20 2QR, UK
Bioorganic & Medicinal Chemistry (1998),
6(1), 1-8

SOURCE: CODEN: BMECEP; ISSN: 0968-0896

Elsevier Science Ltd.

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

Journal
English

AB The synthesis of a series of 2,4-disubstituted morpholines is described and their affinities at human dopamine receptors reported. The orally bioavailable 7-azaindole compound 1 has nanomolar affinity at the hD4 receptor with > 1000-fold selectivity over the hD2 receptor.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:828046 CAPLUS Full-text

DOCUMENT NUMBER: 123:306370

ORIGINAL REFERENCE NO.: 123:54623a, 54626a

TITLE: The pharmacology of SCH 50911: a novel, orally-active

GABA-B receptor antagonist

AUTHOR(S): Bolser, Donald C.; Blythin, David J.; Chapman, Richard

W.; Egan, Robert W.; Hey, John A.; Rizzo,

Charles;

Kuo, Shen-Chun; Kreutner, William

CORPORATE SOURCE: Schering-Plough Res. Inst., Kenilworth, NJ, USA

SOURCE:
Therapeutics

Journal of Pharmacology and Experimental

(1995), 274(3), 1393-8
CODEN: JPETAB; ISSN: 0022-3565

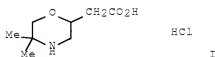
PUBLISHER:
DOCUMENT TYPE:

Williams & Wilkins

LANGUAGE:

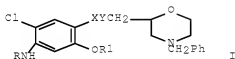
English

GI



AB Expts. were conducted to characterize the pharmacol. of SCH 50911 ((+)-5,5-dimethyl-2-morpholineacetic acid hydrochloride, I), a structurally novel GABA-B receptor antagonist. Although more potent GABA-B antagonists have been reported, in this study SCH 50911 was compared with CGP 35348, a moderately potent and selective GABA-B antagonist with acceptable in vivo activity. SCH 50911 was more potent to inhibit the binding of GABA to the GABA-B receptor in rat brain (IC₅₀ = 1.1 μM) than CGP 35348 (IC₅₀ = 62 μM). SCH 50911 had no binding affinity for GABA-A, histamine H₁, histamine H₃, dopamine D₁, dopamine D₂, serotonin 5-HT₂, or muscarinic m₁, m₂, or m₄ receptors. However, SCH 50911 (IC₅₀ = 2.2 μM) was active in a nonspecific muscarinic receptor binding assay, but was devoid of muscarinic agonist or antagonist activity in the isolated guinea pig ileum. SCH 50911 blocked inhibitory responses to baclofen of the guinea pig trachea in a competitive manner (pA₂ = 5.8 ± 0.004). CGP 35348 was 19-fold less potent in this assay (pA₂ = 4.6 ± 0.15). In vivo, SCH 50911 (ED₅₀ = 2.9 mg kg⁻¹, s.c.) and CGP 35348 (ED₅₀ = 5.8 mg kg⁻¹, s.c.) blocked the antitussive effects of baclofen in the guinea pig. In the cat, both SCH 50911 (10 mg kg⁻¹, i.v.) and CGP 35348 (10 mg kg⁻¹, i.v.) shifted the antitussive dose response relationship for baclofen to the right. Baclofen-induced respiratory depression was blocked by s.c. (ED₅₀ = 0.63 mg kg⁻¹, i.p. (ED₅₀ = 1.9 mg kg⁻¹), or oral (ED₅₀ = 3 mg kg⁻¹) administration of SCH 50911. CGP 35348 also blocked the respiratory depressant effect of baclofen but was 3-9 fold less potent than SCH 50911 by these routes of administration. SCH 50911 (50 μg, i.c.v.) completely blocked respiratory depression by baclofen indicating activity at GABA-B receptors in the CNS. The (-) enantiomer of SCH 50911 was inactive as a GABA-B antagonist. SCH 50911 is a selective, competitive, and orally active GABA-B receptor antagonist. Both central and peripheral GABA-B receptors are blocked by SCH 50911 and this antagonist is more potent than CGP 35348.

ORIGINAL REFERENCE NO.: 123:61011a,61014a
 TITLE: Synthesis and gastroprokinetic activity of
 N-(4-amino-5-chloro-2-methoxyphenyl)-4-benzyl-
 2-morpholineacetamide and related compounds
 AUTHOR(S): Kato, S.; Morie, T.; Yoshida, N.; Fujiwara,
 I.; Kon, T.
 CORPORATE SOURCE: Exploratory Research Laboratories, Dainippon
 Pharmaceutical Co Ltd, Osaka, 564, Japan
 SOURCE: European Journal of Medicinal Chemistry (1995
), 30(7-8), 609-16
 CODEN: EJMCA5; ISSN: 0223-5234
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Benzamide derivs. I (XY = CONH; R = H; R1 = Me, Et) show potent gastroprokinetic activity. To exam. the effect of reversal of the amide linkage, I (XY = NHCO; R = H, acyl, MeSO2; R1 = Me) were prepared and evaluated for gastroprokinetic activity by determining their effects on gastric emptying of a phenol red semisolid meal and a serotonin-4 receptor binding assay. Reversal of the amide bond decreased the activity. A mol. superposition procedure, using computer graphics, suggested that the location of the morpholine ring and N-benzyl group is crucial for activity.

L44 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1995:772766 CAPLUS Full-text
 DOCUMENT NUMBER: 123:228200
 ORIGINAL REFERENCE NO.: 123:40767a,40770a
 TITLE: Morpholine derivatives as dopamine receptor
 subtype ligands and their preparation,
 compositions,
 and use
 INVENTOR(S): Leeson, Paul David; Showell, Graham Andrew
 PATENT ASSIGNEE(S): Merck Sharp and Dohme Ltd., UK
 SOURCE: PCT Int. Appl., 36 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9514690	A1	19950601	WO 1994-GB2557
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MN, MW,
NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA,
US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
IT, LU,
MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,
NE, SN,
TD, TG

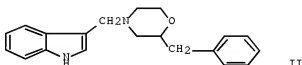
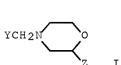
AU 9510719	A	19950613	AU 1995-10719
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AU 680320 B2 19970724
EP 730593 A1 19960911 EP 1995-901522

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL,
PT, SE
US 5614518 A 19970325 US 1996-647926

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PRIORITY APPLN. INFO.: GB 1993-24018 A
19931123 <--
WO 1994-GB2557 W

19941121 <--
OTHER SOURCE(S): CASREACT 123:228200; MARPAT 123:228200
GI



AB A class of substituted morpholine derivs. is disclosed, specifically I [Y = (un)substituted bicyclic heteroarom. ring system containing 1 or 2 N atoms, the ring system comprising a six-membered aromatic or heteroarom. ring fused to a five- or six-membered heteroarom. ring; Z = (un)substituted arylalkyl, aryloxymethyl or arylalkoxyethyl], and their salts and prodrugs. I are ligands for dopamine receptor subtypes, and are therefore useful in the treatment and/or prevention of a variety of disorders of the dopamine system, in particular schizophrenia. For example, condensation of 3-[(dimethylamino)methyl]indole with (R,S)-2-(phenylmethyl)morpholine by heating in refluxing toluene for 16 h gave 92% title compound II. Fourteen examples of I and several salts were prepared, and all were found to have K_i of < 1.5 μM for displacement of [3H]-spiperone from human dopamine D₄ receptors in a binding assay.

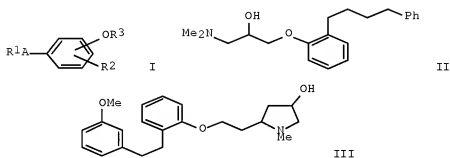
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
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RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L44 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:763484 CAPLUS Full-text
DOCUMENT NUMBER: 123:169510
ORIGINAL REFERENCE NO.: 123:30259a,30262a
TITLE: Phenoxyalkylamines, -pyrrolidines and -
piperidines for
the treatment and prevention of circulatory
diseases
and psychosis.
INVENTOR(S): Fujimoto, Koichi; Tanaka, Naoki; Asai,
Fumitoshi; Ito,
Tomiyoshi; Koike, Hiroyuki
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 218 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 600717	A1	19940608	EP 1993-309570	
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AU 666590	B2	19960215		
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EP 844000	A1	19980527	EP 1997-114529	
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MC, PT, IE				
CZ 283720	B6	19980617	CZ 1993-2582	
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19950105 <--				
FI 9800816	A	19980409	FI 1998-816	
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FI 106551	B1	20010228		
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			JP 1992-338307	A
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			EP 1993-309570	A3
19931130 <--				
			FI 1993-5341	A
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			US 1993-159744	B1
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OTHER SOURCE(S):		CASREACT 123:169510; MARPAT 123:169510		
GI				

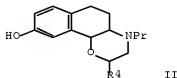
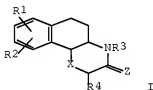


AB Phenoxyalkylamines I [R1 = aryl; R2 = H, alkyl, alkoxy, halo, cyano; R3 = group BNR4R5; R4, R5 = H, alkyl; R4R5 = together with the N form heterocyclic group; B = alkylene, group CH2CH(OR6)CH2; R6 = H, H, alkanoyl, arylcarbonyl, group DR7; D = single bond, alkylene; R7 = heterocyclic group; A = alkylene] were disclosed as serotonergic S2 and/or dopaminergic D2 antagonists. Claimed example compds. are 3-(dimethylamino)-1-[2-(4-phenylbutyl)phenoxy]-2-propanol (II) and 4-hydroxy-1-methyl-2-[2-[2-(3-methoxyphenyl)ethyl]phenoxy]pyrrolidine (III). I and pharmaceutically acceptable salts and esters thereof are useful

for the treatment and prevention of circulatory diseases and psychosis.

L44 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:483352 CAPLUS Full-text
DOCUMENT NUMBER: 121:83352
ORIGINAL REFERENCE NO.: 121:14985a,14988a
TITLE: Preparation of naphthoxazines and analogs as
dopaminergic agonists
INVENTOR(S): Peck, James VanOlden; Minasakanian, Gevork
PATENT ASSIGNEE(S): Whitby Research, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

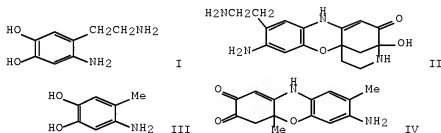
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9324471	A1	19931209	WO 1993-US5305	
19930602 <--				
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL,				
PT, SE				
PRIORITY APPLN. INFO.:			US 1992-889940	A
19920602 <--				
OTHER SOURCE(S):		MARPAT 121:83352		
GI				



AB Title compds. [I; R1,R2 = H, OH, alkoxy, O2CR5, etc.; R3 = alkyl; R4 = (CH2)nCO2R6, (CH2)nCHRR7; R = (hetero)aryl; R5 = alkyl, aryl; R6 = H, alkyl; R7 = H, alkyl, alkoxy, alkanoyloxy; X = CH2, O, S, NH, etc.; Z = H2, O, S; n = 0-4] were prepared. Thus, trans-1a,2,4,4a,5,6-hexahydro-9-methoxy-4-propylnaphth[1,2-b]-1,4-oxazin-3-one was converted in 3 steps to title compound II (R4 = CH2Ph). (+)-II.HCl (R4 = α -CH2Ph) had pKi of 7.50 and 5.89 for binding at dopamine D2 and D1 receptors, resp.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:38668 CAPLUS Full-text
DOCUMENT NUMBER: 118:38668
ORIGINAL REFERENCE NO.: 118:7039a,7042a
TITLE: A new oxidation pathway of the neurotoxin
6-aminodopamine. Isolation and
characterization of a
dimer with a
tetrahydro[3,4a]iminoethanophenoxazine
ring system
AUTHOR(S): Napolitano, Alessandra; D'Ischia, Marco;
Costantini,
Claudio; Prota, Giuseppe
CORPORATE SOURCE: Dep. Org. Biol. Chem., Univ. Naples, Naples,
I-80134,
Italy
SOURCE: Tetrahedron (1992), 48(39), 8515-22
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Oxidation of the neurotoxin 6-aminodopamine (I) is known to proceed through the o-quinone, which undergoes intramol. cyclization to give 5,6-dihydroxyindole. In a re-examination of the reaction, it was found that at concns. of I higher than 5×10^{-3} M a quite different course prevails, leading to the formation of the novel 7-amino-8-(2-aminoethyl)-3-hydroxy-2-oxo-2,3,4,10-tetrahydro[3,4a]iminoethanophenoxazine (II). II was formed by aerobic, chemical (persulfate, periodate) or enzymic (tyrosinase, peroxidase/H₂O₂) oxidation of I. Oxidation of the model compound 5-amino-4-methylcatechol (III) proceeded similarly to I, giving tetrahydrophenoxazinedione IV.

=> d 144 ibib abs 1-9

L44 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:100738 CAPLUS Full-text
 DOCUMENT NUMBER: 144:198849
 TITLE: Novel dosage form comprising modified-release
 and
 immediate-release active ingredients
 INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand,
 Sunil;
 Gupta, Vinod Kumar
 PATENT ASSIGNEE(S): India
 SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part
 of U.S. Ser. No. 630,446.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

	PATENT NO. -----	KIND ----	DATE -----	APPLICATION NO. -----	DATE ----
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20050519 <--	IN 2002MU00697	A	20040529	IN 2002-MU697	
20020805 <--	IN 193042	A1	20040626		
	IN 2002MU00699	A	20040529	IN 2002-MU699	
20020805 <--	IN 2003MU00080	A	20050204	IN 2003-MU80	
20030122	IN 2003MU00082	A	20050204	IN 2003-MU82	
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PRIORITY APPLN. INFO.:				IN 2002-MU697	A
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AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared. The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.

ACCESSION NUMBER: 2005:586215 CAPLUS Full-text
 DOCUMENT NUMBER: 143:120526
 TITLE: Pharmaceutical compositions based on
 anticholinergics
 and additional active ingredients
 INVENTOR(S): Pairat, Michel; Pieper, Michael P.; Meade,
 Christopher
 John Montague; Reichl, Richard; Schmelzer,
 Christel;
 Jung, Birgit
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg,
 Germany
 SOURCE: U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part
 of U.S. Ser. No. 824,391.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 19
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US 20030181478	A1	20030925	US 2003-395777	
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US 20040024007	A1	20040205	US 2003-613783	
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20040414	US 2004-824391	A2
20011023 <--	CA 2001-2436540	A3
20011025 <--	US 2001-40196	B1
20030324	US 2003-395777	A1
20060626	AU 2006-202723	A3

OTHER SOURCE(S): MARPAT 143:120526

AB A pharmaceutical composition comprising an anticholinergic and at least one addnl. active ingredient selected from among corticosteroids, dopamine agonists, PDE-IV inhibitors, NK1-antagonists, endothelin antagonists, antihistamines, and EGFR-kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Among a number of compds. prepared was N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2-[(3-hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-phenylacetamide. Inhalable powders include a formulation containing tiotropium bromide, budesonide, and lactose.

L44 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:513545 CAPLUS Full-text
 DOCUMENT NUMBER: 141:71567
 TITLE: Preparation of 2-phenylmorpholines and related compounds as dopamine agonists in the treatment of sexual dysfunction.
 INVENTOR(S): Allerton, Charlotte Moria Norfor; Baxter, Andrew

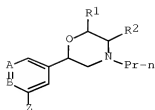
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Douglas; Cook, Andrew Simon; Hepworth, David;

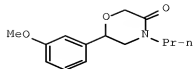
PATENT ASSIGNEE(S): Stephen Kwok-fung
SOURCE: Pfizer Limited, UK; Pfizer Inc.
PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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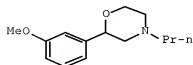
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OTHER SOURCE(S):	MARPAT	141:71567		
GI				



I



II



III

AB Title compds. I [A = C-X, N; B = C-Y, N; R1 = H, alkyl; R2 = H, alkyl; X = H, OH, CONH2, etc.; Y = H, OH, NH2, etc.; Z = H, OH, F, etc.] their enantiomers and pharmaceutically acceptable salts were prepared For example, BH3-THF reduction of lactam II, e.g., prepared from 3-methoxybenzaldehyde in 5-steps, afforded 2-phenylmorpholine III in 84% yield. Compds. I expressed EC50 values < 1000 nM with 10-fold selectivity for D3 over D2, e.g., one example of compound I exhibited an EC50 value of 7.6 nM and 1315.8 fold selectivity for D3 over D2. Compds. I are claimed useful for the treatment of sexual dysfunction, e.g., hypoactive sexual activity, orgasmic disorders, erectile dysfunction, etc.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE

L44 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:392318 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 140:400077
 TITLE: Pharmaceutical combinations including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and their use in treating gastrointestinal and abdominal visceral disorders
 INVENTOR(S): Billstein, Stephan Anthony; Dumovic, Peter; Franco, Nicola; Iwicki, Mark Thomas; Pfannkuche, Hans-Jurgen;
 Jurgens;
 PATENT ASSIGNEE(S): Wilusz, Edward Joseph
 SOURCE: USA
 Ser. No. U.S. Pat. Appl. Publ., 14 pp., Cont. of U.S. 722,784, abandoned.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

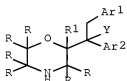
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20040092511	A1	20040513	US 2003-702688	
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US 20080090878	A1	20080417	US 2007-973404	
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19991210 <--				
			US 2000-722784	B1
20001127 <--				
			US 2003-702688	A1
20031106				

AB The invention discloses a combination of a first agent including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and pharmaceutical compns. and formulations containing the combination. The invention also discloses a method for treating a gastrointestinal and abdominal visceral disorder by administering the pharmaceutical compns. to a patient. The pharmaceutical compns. may also be employed as laxatives, to prepare a patient for colonoscopy and to regulate and stabilize enterochromaffin cell secretory, pain and motility mechanisms, afferent fiber activity and GI and lower abdominal smooth muscle cells. The dosage is preferably oral and administration is preferably once or twice a day. The preferred first agent is tegaserod.

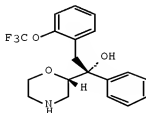
L44 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:182855 CAPLUS Full-text
DOCUMENT NUMBER: 140:217649
TITLE: Preparation of aryl and heteroaryl morpholine derivatives as norepinephrine reuptake inhibitors
INVENTOR(S): Cases-Thomas, Manuel Javier; Haughton, Helen Louise;
Sivi; Lamas-Peteira, Carlos; Ouwerkerk-Mahadevan, Masters, John Joseph; Simmonds, Robin George;
Rudyk, Helene Catherine Eugenie; Walter, Magnus Wilhelm
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004018441	A1	20040304	WO 2003-US23270	

20030818 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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AU 2003268024 A1 20040311 AU 2003-268024
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 20060003998 A1 20060105 US 2005-524921
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US 7354920 B2 20080408
PRIORITY APPLN. INFO.: GB 2002-19687 A
20020823 <--
US 2002-415303P P
20021001 <--
WO 2003-US23270 W
20030818
OTHER SOURCE(S): MARPAT 140:217649
GI



I



II

AB Morpholine derivs. of formula I [R = independently H, alkyl; R1 = H, alkyl; Y = OH, alkoxy; Ar1, Ar2 = (substituted) Ph, (substituted) heteroaryl] are prepared. The compds. are selective inhibitors of the reuptake of norepinephrine. Thus, II.HCl was

prepared from (4-benzylmorpholin-2-yl)-phenylmethanone (preparation given) and 2-(trifluoromethoxy)benzyl bromide. The compds. had Ki values less than 500 nM at the norepinephrine transporter in a scintillation proximity assay.

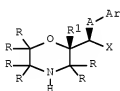
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

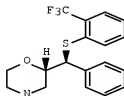
L44 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:182714 CAPLUS Full-text
 DOCUMENT NUMBER: 140:235724
 TITLE: Preparation of benzyl morpholine derivatives capable of selectively inhibiting norepinephrine reuptake
 INVENTOR(S): Walter, Magnus Wilhelm; Clark, Barry Peter; Gallagher, Peter Thaddeus; Haughton, Helen Louise; Rudyk, Helene
 Catherine Eugenie
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 81 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017977	A2	20040304	WO 2003-US23269	
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WO 2004017977	A3	20040401		
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 AT 413882 T 20081115 AT 2003-751812
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 US 20060035894 A1 20060216 US 2005-524650
 20050217 <--
 US 7384941 B2 20080610
 PRIORITY APPLN. INFO.: GB 2002-19690 A
 20020823 <-- US 2002-415328P P
 20021001 <-- WO 2003-US23269 W
 20030818
 OTHER SOURCE(S): MARPAT 140:235724
 GI



I



II

AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl group, a cycloalkyl group or cycloalkylmethyl group] and pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared via substitution of (2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (preparation given) with 2-trifluoromethylthiophenol with subsequent debenzoylation. I have been found to exhibit a Ki value less than 500nM at the norepinephrine transporter as determined by scintillation proximity assays. In addition, I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE

DOCUMENT NUMBER: 140:93935
 TITLE: N-benzyl-3-phenyl-3-heterocyclyl-propionamide
 compounds as tachykinin/serotonin reuptake
 inhibitors
 INVENTOR(S): Alvaro, Giuseppe; Cardullo, Francesca;
 D'adamo,
 Lucilla; Piga, Elisabetta; Seri, Catia
 PATENT ASSIGNEE(S): Glaxo Group Limited, UK
 SOURCE: PCT Int. Appl., 105 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005255	A1	20040115	WO 2003-EP7126	
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EP 1517894	A1	20050330	EP 2003-740413	
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501182	T	20060112	JP 2004-518695	
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AT 338748	T	20060915	AT 2003-740413	
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ES 2271606	T3	20070416	ES 2003-740413	
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US 20060058348	A1	20060316	US 2005-521159	
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20020703 <--				

20030702

OTHER SOURCE(S): MARPAT 140:93935
GI* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB Title compds. I [R = halo, alkyl, CN, alkoxy, etc.; R1 = 5-6-membered heteroaryl, etc.; R2 = H, alkyl; R3-4 = H, alkyl, cycloalkyl; R5 = CF3, SOO-2, etc.; L = single or double bond; n = 1-3; m = 0-3] are prepared For instance, 4-[2-Carboxy-1-(4-fluorophenyl)ethyl]piperidine-1-carboxylic acid tert-Bu ester (preparation given) is coupled to [3,5-bis(trifluoromethyl)benzyl]methylamine and deprotected to give II. Compds. of the invention have pKi = 10.44 to 7.54 for the NK1 receptor. I are useful in the treatment of conditions mediated by tachykinins and/or by selective inhibition of serotonin reuptake transporter protein.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:2708 CAPLUS Full-text

DOCUMENT NUMBER: 140:53450

TITLE: Serotonin reuptake inhibitor combination
with a GABAB receptor antagonist for the

treatment of

depression and other disorders

INVENTOR(S):

Mork, Arne; Cremers, Thomas Ivo Franciscus

Hubert;

Willigers, Sandra

PATENT ASSIGNEE(S):

H. Lundbeck A/S, Den.

SOURCE:

PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
2004000326	A1	20031231	WO 2003-DK412	

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 CA 2490638 C 20080122
 CA 2579520 A1 20031231 CA 2003-2579520
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 JP 2005533069 T 20051104 JP 2004-514582
 20030619 <--
 AT 357920 T 20070415 AT 2003-729907
 20030619 <--
 ES 2282632 T3 20071016 ES 2003-729907
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 NZ 536624 A 20080430 NZ 2003-536624
 20030619 <--
 CN 101358379 A 20090204 CN 2008-10215884
 20030619 <--
 ZA 2004009278 A 20060426 ZA 2004-9278
 20041118 <--
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 20041213 <--
 MX 2004012693 A 20050323 MX 2004-12693
 20041215 <--
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 US 2002-390851P P
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 CA 2003-2490638 A3
 CN 2003-814438 A3
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20030619

AB The invention relates to the use of a compound, which is a serotonin reuptake inhibitor, and another compound, which is a GABAB receptor antagonist, inverse agonist or partial agonist for the preparation of a pharmaceutical composition for the treatment of depression, anxiety disorders and other affective disorders, such as generalized anxiety disorder, panic anxiety, obsessive compulsive disorder, acute stress disorder, post traumatic stress disorder and social anxiety disorder, eating disorders such as bulimia, anorexia and obesity, phobias, dysthymia, premenstrual syndrome, cognitive disorders, impulse control disorders, attention deficit hyperactivity disorder, drug abuse or any other disorder responsive to serotonin reuptake inhibitors.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L44 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:932584 CAPLUS Full-text
 DOCUMENT NUMBER: 139:17446
 TITLE: SSR240600 [(R)-2-(1-{2-[4-{2-[3,5-bis(trifluoromethyl)phenyl]acetyl}-2-(3,4-dichlorophenyl)-2-morpholinyl]ethyl}-4-piperidinyl)-2-methylpropanamide], a centrally active nonpeptide antagonist of the tachykinin neurokinin 1 receptor:
 II. Neurochemical and behavioral characterization
 AUTHOR(S): Steinberg, Regis; Alonso, Richard; Rouquier, Liliane;
 Desvignes, Christophe; Michaud, Jean-Claude; Cudennec,
 Annie; Jung, Mireille; Simiand, Jacques; Griebel, Guy;
 Emonds-Alt, Xavier; Le Fur, Gerard; Soubrie, Philippe
 CORPORATE SOURCE: C.N.S. Research Department, Sanofi-Synthelabo Recherche, Montpellier, Fr.
 SOURCE: Journal of Pharmacology and Experimental Therapeutics
 (2002), 303(3), 1180-1188
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: American Society for Pharmacology and Experimental
 Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB SSR240600 , a new nonpeptide tachykinin neurokinin 1 (NK1) receptor antagonist, was evaluated against the neurochem., electrophysiol., and behavioral effects provoked by direct activation of brain tachykinin NK1 receptors or by stress in guinea pigs. SSR240600 (0.1-10 mg/kg i.p. or p.o.) antagonized the excitatory effect of i.c.v. infusion of

[Sar9, Met(02)11] substance P (SP) on the release of acetylcholine in the striatum of anesthetized and awake guinea pigs. This antagonistic action was still observed after repeated administration of SSR240600 (5 days, 10 mg/kg p.o., once a day). SSR240600 (10 mg/kg i.p.) inhibited the phosphorylation of the cAMP response element-binding protein in various brain regions induced by i.c.v. administration of [Sar9, Met(02)11]SP. In slice preps., neuronal firing of the locus coeruleus (LC) neurons elicited by the application of [Sar9, Met(02)11]SP was suppressed by SSR240600 at 100 nM. Norepinephrine release in the prefrontal cortex, elicited either by an intra-LC application of [Sar9, Met(02)11]SP or by an i.c.v. administration of corticotropin-releasing factor, was reduced by SSR240600 (0.3-1 mg/kg and 1-10 mg/kg i.p., resp.). SSR240600 (1-10 mg/kg i.p.) inhibited vocalizations induced in adult guinea pigs by an i.c.v. administration of the NK1 receptor agonist, GR73632 [D-Ala-[L-Pro9, Me-Leu8] substance P(7-11)]. Furthermore, SSR240600 (1-10 mg/kg i.p.) inhibited distress vocalizations produced in guinea pig pups by maternal separation. SSR240600 also reduced maternal separation-induced increase in the number of neurons displaying NK1 receptor internalization in the amygdala. Finally, SSR240600 counteracted the increase in body temperature induced by isolation stress. In conclusion, SSR240600 is able to antagonize various NK1 receptor-mediated as well as stress-mediated effects in the guinea pig.

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

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which fields in the current file have left truncation, enter "HELP
SFIELDS" at an arrow prompt (=>).

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L20 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:732631 CAPLUS Full-text
DOCUMENT NUMBER: 143:193912
TITLE: Preparation of piperidine derivatives as
estrogen antagonists in the uterus that do not
stimulate the ovaries for treating endometriosis and uterine
leiomyoma
INVENTOR(S): Dally, Robert Dean; Dodge, Jeffrey Alan;
Hummel, Conrad Wilson; Jones, Scott Alan; Shepherd,
Timothy Alan; Wallace, Owen Brendan; Weber, Wayne
Woodrow, II
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005073205	A1	20050811	WO 2005-US21	
20050118				
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MR, NE, SN, TD, TG
 EP 1709022 A1 20061011 EP 2005-704875
 20050118
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 MC, PT,
 IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
 US 20070111988 A1 20070517 US 2006-597008
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 PRIORITY APPLN. INFO.: US 2004-538441P P
 20040122 US 2004-582945P P
 20040625 WO 2005-US21 W
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 OTHER SOURCE(S): CASREACT 143:193912; MARPAT 143:193912
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB The present invention relates to alcs. (shown as I; variables defined below; e.g. [4-[6-methoxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]phenyl]methanol) or a pharmaceutical acid addition salt thereof and carboxy compds. (shown as II; variables defined below; e.g. 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]-N,N-dimethylbenzamide hydrochloride) or a pharmaceutical salt thereof as selective estrogen receptor modulators, useful, e.g., for treating endometriosis and/or uterine leiomyoma/leiomyomata. Other similar Markush formulas for claimed compds. are given in the claims. In the Ishikawa cell proliferation assay, cell proliferation (using an alkaline phosphatase readout) was measured in both an agonist mode in the presence of I or II alone, and in an antagonist mode in which the ability of I or II to block estradiol stimulation of growth was measured. In the agonist mode, the compds. of 14 examples were tested and are less stimulatory than tamoxifen. For example, 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]-N,N-dimethylbenzamide hydrochloride had a relative % efficacy of 15% and 2-hydroxy-5-[4-[2-(piperidin-1-yl)ethoxy]phenyl]-5H-6-oxachrysene-7-carboxylic acid trifluoroacetate had a relative % efficacy of 25%. In the antagonist mode, these same compds. inhibited greater than at least 80% of the 1 nM estradiol response. For example, 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]-N,N-dimethylbenzamide hydrochloride had an IC50 of 9 nM and a % efficacy of 95% and 2-hydroxy-5-[4-[2-(piperidin-1-yl)ethoxy]phenyl]-5H-6-oxachrysene-7-carboxylic acid trifluoroacetate had an IC50 of 36 nM and a % efficacy of 92%. Results of a 3-day rat uterus antagonist assay are also reported. One example compound was tested in a 4-day OVX rat uterine agonist assay and did not cause any dose-related statistically significant increase in uterine eosinophil peroxidase activity. Two example compds. did not significantly elevate circulating estradiol or LH levels. For I: m = 0-2; R0 is

H, F or OH; R1 is H, SO2(n-C4-C6 alkyl) or COR4; R2 is H or Me provided that if m is 1 or 2, then R2 must be H and that if m is 0, then R2 must be Me; X is O or NR5; Y is S or CH:CH; R4 is Cl-C6 alkyl, Cl-C6 alkoxy, NR6R7, phenoxy, or Ph (un)substituted with halo; R5 is H or Cl-C6 alkyl; R6 and R7 = H, Cl-C6 alkyl or phenyl; R is H and X1 is O, CH2 or CO or R combines with X1 to form III (X2 is O or S); and R3 and R3a = H or Cl-C6 alkyl. For II: m = 0-2; R1 is H, SO2(n-C4-C6 alkyl) or COR4; R2 is H or Me provided that if m is 1 or 2, then R2 must be H and that if m is 0, then R2 must be Me; X is O or NR5; Y is S or CH:CH; R4 is Cl-C6 alkyl, Cl-C6 alkoxy, NR6R7, phenoxy, or Ph (un)substituted with halo; R5 is H or Cl-C6 alkyl; R6 and R7 = H, Cl-C6 alkyl or phenyl; R is H and X1 is O, CH2 or CO or R combines with X1 to form IV (X2 is O or S); R3b is NR8R9 or OR10 or when R is H, R3b may combine with the Ph with which it is attached to form V (W and W1 are CH2 or C:O provided that at least one of W or W1 must be C:O; X3 is NR11 or O; R8 and R9 = H or Cl-C6 alkyl or R8 and R9 may combine with the N to which they are both attached to form a morpholino, pyrrolidino or piperidino ring; R10 and R11 = H or Cl-C6 alkyl). Although the methods of preparation are not claimed, .apprx.70 example preps. are included. For example, 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]benzamide hydrochloride was prepared (88 %) by HCl treatment of 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]benzonitrile hydrochloride, which was prepared (98 %) by coupling trifluoromethanesulfonic acid 6-methoxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl ester (preparation described) with 3-cyanophenylboronic acid followed by conversion of the OMe to OH group.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

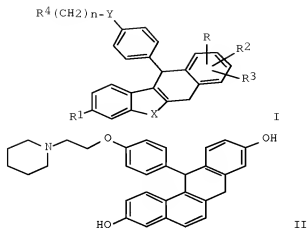
RE FORMAT

L20 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:292023 CAPLUS Full-text
 DOCUMENT NUMBER: 140:303419
 TITLE: Preparation of dihydro-dibenzo(a)anthracenes as

selective estrogen receptor modulators
 INVENTOR(S): Wallace, Owen Brendan
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004029047	A1	20040408	WO 2003-US26304	
20030922				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,			

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LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG
CA 2497627 A1 20040408 CA 2003-2497627
20030922
AU 2003265581 A1 20040419 AU 2003-265581
20030922
EP 1546139 A1 20050629 EP 2003-798700
20030922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003014594 A 20050809 BR 2003-14594
20030922
CN 1684958 A 20051019 CN 2003-822675
20030922
JP 2006508066 T 20060309 JP 2004-539841
20030922
US 20060122386 A1 20060608 US 2005-527527
20050311
US 7119206 B2 20061010
MX 2005003166 A 20050608 MX 2005-3166
20050323
IN 2005KN00711 A 20060616 IN 2005-KN711
20050425
PRIORITY APPLN. INFO.: US 2002-413609P P
20020925
WO 2003-US26304 W
20030922
OTHER SOURCE(S): MARPAT 140:303419
GI



AB Dihydro-dibenzo(a)anthracenes of formula I [R1 = H, OH, alkoxy, benzoyloxy, acyloxy, OSO2alkyl, etc.; R, R2, R3 = H, OH, alkoxy, benzoyloxy, acyloxy, OSO2alkyl, halo; R4 = 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino; n = 2-3; X = S, CH=CH; Y = O, S, NH, NMe, CH2] are prepared for pharmaceutical compns., optionally in combination with estrogen and progestin, for inhibiting a disease associated with estrogen deprivation or a disease associated with an aberrant physiol. response to endogenous estrogen. Thus, II.TFA was prepared from (2,6-dimethoxynaphthalen-1-yl)-[4-(2-piperidin-1-yloxy)phenyl]methanone and 3-methoxybenzylzinc chloride. II had IC50 of 2 nM against MCF-7 breast adenocarcinoma cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L20 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:80700 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:128294

TITLE: Preparation of dihydrodibenzo[b,e]oxepine based

selective estrogen receptor modulators for

treatment

of estrogen related diseases

INVENTOR(S): Wallace, Owen Brendan

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

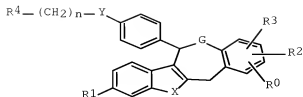
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

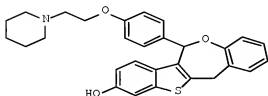
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 WO 2004009603 A1 20040129 WO 2003-US19554
 20030711
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 CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
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 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI,
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG
 AU 2003281632 A1 20040209 AU 2003-281632
 20030711
 EP 1527076 A1 20050504 EP 2003-742113
 20030711
 EP 1527076 B1 20051228
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 JP 2005538091 T 20051215 JP 2004-523010
 20030711
 AT 314375 T 20060115 AT 2003-742113
 20030711
 ES 2253691 T3 20060601 ES 2003-742113
 20030711
 US 20050240017 A1 20051027 US 2005-521137
 20050112
 US 7067510 B2 20060627
 US 20060142267 A1 20060629 US 2006-276203
 20060217
 US 7375229 B2 20080520
 PRIORITY APPLN. INFO.: US 2002-398538P P
 20020724 WO 2003-US19554 W
 20030711 US 2005-521137 A3
 20050112
 OTHER SOURCE(S): MARPAT 140:128294
 GI



I



II

AB Title compds. I [wherein R1 = H, OH, alkoxy, OCOPh, alkanoyloxy, or alkylsulfonyloxy; R0, R2, and R3 = independently H, OH, alkoxy, OCOPh, alkanoyloxy, alkylsulfonyloxy, or halo; R4 = piperidinyl, (un)substituted pyrrolidinyl, morpholine, dialkylamino, or piperidinyl; n = 2 or 3; X = S or CH=CH; G = O, S, SO, SO2, or NR5; R5 = H or alkyl; Y = O, S, NH, NMe, or CH2; or pharmaceutically acceptable salts thereof] were prepared as selective estrogen receptor (ER) modulators. For example, reaction of 2-methoxybenzylmagnesium chloride with (2-dimethylamino-6-methoxybenzo[b]thiophen-3-yl)[4-[2-(piperidinyl-1-yl)ethoxy]phenyl]methanone in THF, followed by deprotection using HCl/ether in CH2Cl2 gave [6-hydroxy-2-(2-hydroxybenzyl)benzo[b]thiophen-3-yl][4-[2-(piperidin-1-yl)ethoxy]phenyl]methanone (54%). Cyclization with DIBAL in THF provided the 5,11-dihydro-6-oxa-12-thiadibenzo[a,f]azulene II (62%). In competition binding assays, the latter showed activity with Ki values of 1 nM at both of the ER α and ER β receptors. Thus, I are useful in pharmaceutical compns., optionally in combination with estrogen and progestin, for inhibiting a disease associated with estrogen deprivation or an aberrant physiolo. response to endogenous estrogen, such as bone loss, breast cancer, endometriosis, or uterine fibrosis (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L20 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:282118 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:304300

TITLE: Preparation and antiviral activity of substituted

piperazinyloxoacetylindole derivatives

INVENTOR(S): Wallace, Owen B.; Wang, Tao; Yeung, Kap-Sun; Pearce, Bradley C.; Meanwell, Nicholas A.;

Qiu, Zhilei; Fang, Haiquan; Xue, Qiufen May; Yin, Zhiwei

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 182 pp., Cont.-in-part
of U.S.

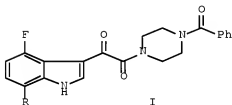
Ser. No. 888,686.

CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20030069245	A1	20030410	US 2001-27612	
20011219				
US 6573262	B2	20030603		
PRIORITY APPLN. INFO.:			US 2000-217444P	P
20000710				
			US 2001-265978P	P
20010202				
			US 2001-888686	A2
20010625				
OTHER SOURCE(S):	MARPAT	138:304300		
GI				



AB Piperazinyl oxoacetylindole derivs., e.g. I (R = Ph), were prepared and tested as human antiviral agents, specifically to be used for treating HIV and AIDS. Thus, bromoindole I (R = Br) (II) reacted with tri-n-butylphenyltin to give I (R = Ph). Furthermore, II was prepared by reacting 2-bromo-5-fluoronitrobenzene with vinylmagnesium bromide, which gave 4-fluoro-7-bromoindole. The latter compound was then added to Et chlorooxoacetate to give the acylated adduct which was hydrolyzed to the acid and aminated with N-benzoylpiperazine. Testing of these compds. indicated that they possess unique antiviral activity; and they are proposed to be used alone or in combination with other antivirals, anti-infectives, immunomodulators or HIV entry inhibitors.

L20 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:906161 CAPLUS Full-text
DOCUMENT NUMBER: 137:384759

TITLE: Preparation of tetrahydroquinolines as
selective estrogen receptor modulators.

INVENTOR(S): Wallace, Owen Brenda;

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2

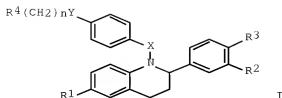
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
20020509	A1	20021128	WO 2002-US11878	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002316036	A1	20021203	AU 2002-316036	
20020509	A1	20040310	EP 2002-746308	
EP 1395563	B1	20060329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004531562	T	20041014	JP 2002-591461	
20020509	T	20060415	AT 2002-746308	
AT 321754	T3	20061001	ES 2002-746308	
20020509	A1	20041028	US 2003-475593	
ES 2259376	B2	20060606		
20020509			US 2001-292704P	P
US 20040215018			WO 2002-US11878	W
20031022				
US 7056931				
PRIORITY APPLN. INFO.: 20010522				
20020509				
OTHER SOURCE(S):	MARPAT	137:384759		
GI				



AB Title compds. (I; R1 = H, OH, alkoxy, PhO2C, alkoxycarbonyl, alkylsulfonyloxy; R2, R3 = H, OH, alkoxy, PhO2C, alkoxycarbonyl, alkylsulfonyloxy, halo; R4 = piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, Me2N, Et2N, (Me2CH)2N, azepinyl; n = 1-3; X = CO, CH2; Y = O, S, NH, NMe, CH2), were prepared. Thus, 6-methoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline (preparation given), 4-(2-piperidin-1-ylethoxy)benzoyl chloride hydrochloride, and Et3N were stirred in CH2Cl2 to give [6-methoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinolin-1-yl]-(4-(2-piperidin-1-ylethoxy)phenyl)methanone. Tested I bound to ER α receptors with K_i = 0.6-87.8 μ M. I, optionally in combination with estrogen or progestin, are useful for inhibiting a disease associated with estrogen deprivation and for inhibiting a disease associated with an aberrant physiol. response to endogenous estrogen.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:51452 CAPLUS Full-text

DOCUMENT NUMBER: 136:118470

TITLE: Preparation of substituted indoleoxoacetyl piperazines

with antiviral activity against HIV-1
INVENTOR(S): Wallace, Owen B.; Wang, Tao; Yeung, Kap-Sun; Pearce, Bradley C.; Meanwell, Nicholas A.;

Qiu, Zhilei; Fang, Haiquan; Xue, Qiu Fen May; Yin, Zhiwei

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Squibb Bristol

Myers Co
SOURCE: PCT Int. Appl., 277 pp., which
CODEN: PIXXD2

DOCUMENT TYPE: Patent

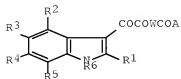
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 WO 2002004440 A1 20020117 WO 2001-US20300
 20010626
 WO 2002004440 A9 20051103
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 LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
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 TR, BF,
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 CA 2413044 A1 20020117 CA 2001-2413044
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 EP 1299382 A1 20030409 EP 2001-946715
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 EP 1299382 B1 20050921
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
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 HU 2003003082 A2 20031229 HU 2003-3082
 20010626
 HU 2003003082 A3 20070828
 JP 2004502768 T 20040129 JP 2002-509305
 20010626
 AU 2001268727 B2 20050324 AU 2001-268727
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 AT 304853 T 20051015 AT 2001-946715
 20010626
 ES 2250422 T3 20060416 ES 2001-946715
 20010626
 PRIORITY APPLN. INFO.: US 2000-217444P P
 20000710 US 2001-265978P P
 20010202 WO 2001-US20300 W
 20010626
 OTHER SOURCE(S): MARPAT 136:118470
 GI



AB Indoleoxoacetyl piperazines I [A = (un)substituted alkoxy, aryl, heteroaryl; W = (un)substituted piperazino; R1 = H; R2-R5 = H, halogen, CN, NO2, (un)substituted NH2, OH, (un)substituted alkyl, cycloalkyl, alkoxy, CO2H, acyl, carbamoyl, amidino, aryl, heteroaryl, heterocyclic; R6 = H, alkyl] and their 2,3-dihydroindole analogs were prepared for use as virucides in the treatment of HIV and AIDS. Thus, 2-bromo-5-fluoronitrobenzene was cyclized with CH2:CHMgBr to give 4-fluoro-7-bromoindole, which was treated with ClCOCO2Et, followed by ester hydrolysis to give 4-fluoro-7-bromo-3-indoleglyoxylic acid. This acid was amidated with N-benzoylpiperazine and treated with PhSnBu3 to give I [A = R5 = Ph, W = piperazino, R1, R3, R4, R6 = H, R2 = F]. This compound gave >98% inhibition of HIV-1 infection in HeLa cells.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s ?morpholin? and (central nervous system or CNS)

82865 ?MORPHOLIN?
454961 CENTRAL
40 CENTRALS
454990 CENTRAL
(CENTRAL OR CENTRALS)
241273 NERVOUS
2737058 SYSTEM
1472680 SYSTEMS
3691947 SYSTEM
(SYSTEM OR SYSTEMS)
91503 CENTRAL NERVOUS SYSTEM
(CENTRAL(W)NERVOUS(W)SYSTEM)

44185 CNS
L21 1633 ?MORPHOLIN? AND (CENTRAL NERVOUS SYSTEM OR CNS)

=> s ?morpholin? and ?neuro?

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635610 ?NEURO?

L22 3401 ?MORPHOLIN? AND ?NEURO?

=> s ?morpholin? and hormon?

82865 ?MORPHOLIN?
450199 HORMON?

L23 987 ?MORPHOLIN? AND HORMON?

=> s ?morpholin? and CYP2D6

82865 ?MORPHOLIN?
3489 CYP2D6

L24 19 ?MORPHOLIN? AND CYP2D6

=> d 124 ibib abs 10-19

L24 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:151666 CAPLUS Full-text
DOCUMENT NUMBER: 145:188776

TITLE: A medicinal-chemistry-guided approach to selective and drug-like sigma 1 ligands

AUTHOR(S): Corbera, Jordi; Vano, David; Martinez, Daniel; Vela, Jose M.; Zamanillo, Daniel; Dordal, Alberto; Andreu, Francesc; Hernandez, Enric; Perez, Raquel; Escriche, Marisol; Salgado, Leonardo; Yeste, Sandra; Serafini, Maria Teresa; Pascual, Rosalia; Alegre, Julia; Calvet, Maria Came; Cano, Nuria; Carro, Monica; Buschmann, Helmut; Holenz, Jorg

CORPORATE SOURCE: Department of Medicinal Chemistry, Laboratorios Dr. Esteve S.A., Barcelona, 08041, Spain

SOURCE: ChemMedChem (2006), 1(1), 140-154
CODEN: CHEMGX; ISSN: 1860-7179

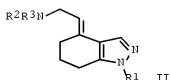
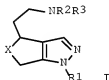
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:188776

GI



AB Based on a medicinal-chemical-guided approach, three novel series of drug-like cycloalkyl-annelated pyrazoles I [X = CH₂, CH₂CH₂; R₁ = Me, Ph, 4-FC₆H₄, 3,4-Cl₂C₆H₃; R₂ = R₃ = Et; R₂ = Me, R₃ = PhCH₂; R₂R₃N = piperidinyl, morpholinyl, 4-benzyl-1-piperazinyl, 1,3-dihydroisoindolyl, etc.] and II were synthesized and display high affinity (pK_i > 8) for the σ₁ receptor. Structure-affinity relationships were established, and the different scaffolds were optimized with respect to σ₁ binding and selectivity vs. the σ₂ receptor and the hERG channel, resulting in selective compds. that have K_i values (for σ₁) in the subnanomolar range. Selected compds. were screened for cytochrome P 450 inhibition (CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4), metabolic stability (rat and human liver microsomes), and cell-membrane permeability (Caco-2). They showed favorable in vitro ADME properties as well as favorable calculated drug-like and exptl. physicochem. properties. Furthermore, compds. I [X =

(CH2)2; R1 = Ph; R2R3N = morpholinyl and II (R1 = Ph; R2R3N = piperidinyl) displayed high selectivity (affinity) for the α_1 receptor against a wide range of other receptors (>60). With these valuable tool compds. in hand, the role of the α_1 receptor in relevant animal models corresponding to such medicinal indications as drug abuse, pain, depression, anxiety, and psychosis will be further explored.

REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR

THE RE THIS RECORD. ALL CITATIONS AVAILABLE IN
FORMAT

L24 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:603072 CAPLUS Full-text

DOCUMENT NUMBER: 143:146468

TITLE: Beneficial effects of a new 20-

hydroxyeicosatetraenoic

acid synthesis inhibitor, TS-011 [N-(3-chloro-

4-

morpholin

-4-yl)phenyl-N'-hydroxyimidoformamide], on

hemorrhagic

and ischemic stroke

AUTHOR(S):

Miyata, Noriyuki; Seki, Takayuki; Tanaka, Yu;

Omura,

Tomohiro; Taniguchi, Kazuo; Doi, Mariko;

Bandou,

Kagumi; Kametani, Shunichi; Sato, Masakazu;

Okuyama,

Shigeru; Cambj-Sapunar, Liana; Harder, David

R.;

Roman, Richard J.

CORPORATE SOURCE:

Medicinal Research Laboratories, Taisho

Pharmaceutical

Co., Ltd., Saitama, Japan

SOURCE:

Journal of Pharmacology and Experimental

Therapeutics

(2005), 314(1), 77-85

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER:

American Society for Pharmacology and

Experimental

Therapeutics

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The present study characterized the effects of TS-011 on the metabolism of arachidonic acid by human and rat renal microsomes and the inhibitory effects of this compound on hepatic cytochrome P 450 enzymes involved in drug metabolism. The effects of TS-011 on the fall in cerebral blood flow following subarachnoid hemorrhage (SAH) and in reducing infarct size in ischemic stroke models were also examined since 20-HETE may contribute to the development of cerebral vasospasm. TS-011 inhibited the synthesis of 20-HETE by human renal microsomes and recombinant CYP4A11 and 4F2, 4F3A, and 4F3B enzymes with IC50 values around 10 to 50 nM. It had no effect on the activities of CYP1A, 2C9, 2C19, 2D6, or

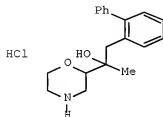
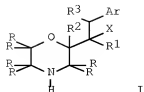
3A4 enzymes. TS-011 inhibited the synthesis of 20-HETE by rat renal microsomes with an IC50 of 9.19 nM, and it had no effect on epoxigenase activity at a concentration of 100 µM. TS-011 (0.01-1 mg/kg i.v.) reversed the fall in cerebral blood flow and the increase in 20-HETE levels in the cerebrospinal fluid of rats after SAH. TS-011 also reduced the infarct volume by 35% following transient ischemic stroke and in intracerebral hemorrhage in rats. Injection of 20-HETE (8 or 12 mg/kg) into the carotid artery produced an infarct similar to that seen in the ischemic stroke model. These studies indicate that blockade of the synthesis of 20-HETE with TS-011 opposes cerebral vasospasm following SAH and reduces infarct size in ischemic models of stroke.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:451370 CAPLUS Full-text
 DOCUMENT NUMBER: 142:482071
 TITLE: Preparation of morpholine derivatives as norepinephrine reuptake inhibitors
 INVENTOR(S): Campbell, Gordon Iain; Cases-Thomas, Manuel Javier;
 Man, Teresa; Masters, John Joseph; Rudyk, Helene
 PATENT ASSIGNEE(S): Catherine Eugenie; Walter, Magnus Wilhelm
 SOURCE: Eli Lilly and Company, USA
 PCT Int. Appl., 133 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	----
WO 2005047272	A1	20050526	WO 2004-US32771	
20041028				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,			

	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,		
RO, SE,	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,		
MR, NE,	SN, TD, TG		
	AU 2004289616	A1	20050526 AU 2004-289616
20041028	CA 2544649	A1	20050526 CA 2004-2544649
20041028	EP 1682523	A1	20060726 EP 2004-794209
20041028	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,		
MC, PT,	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,		
PL, SK, HR			
	CN 1878762	A	20061213 CN 2004-80033115
20041028	BR 2004015273	A	20061219 BR 2004-15273
20041028	JP 2007510720	T	20070426 JP 2006-539492
20041028	US 20070083046	A1	20070412 US 2006-577841
20060429	US 7423037	B2	20080909
	MX 2006005226	A	20060720 MX 2006-5226
20060509	KR 2006086408	A	20060731 KR 2006-708999
20060509	KR 783855	B1	20071210
	NO 2006002700	A	20060808 NO 2006-2700
20060612			
PRIORITY APPLN. INFO.:			GB 2003-26148 A
20031110			
			US 2004-535459P P
20040109			
			WO 2004-US32771 W
20041028			
OTHER SOURCE(S):	CASREACT 142:482071; MARPAT 142:482071		
GI			



AB Title compds. I [X = OH, alkoxy, NH₂, etc.; R independently = H, alkyl, with provisions; R₁ = (un)substituted-alkyl, -alkoxy, CN, etc.; R₂ = H, alkyl; R₃ = H, alkyl; Ar = (un)substituted-Ph, -5- to 6-membered heteroaryl] and their pharmaceutically acceptable salts, are prepared and disclosed as norepinephrine reuptake inhibitors. Thus, e.g., II was prepared by conversion of 4-benzyl-morpholine-2-carbonitrile into the resp. carboxylic Et ester followed by amidation with N,N-dimethylhydroxylamine and subsequent Grignard reactions with Me magnesium bromide and 2-phenylbenzyl magnesium bromide followed by debenzoylation and conversion into the HCl salt. The activity of I was evaluated in a CYP2D6 inhibition assay and preferred compds. of the invention exhibited an IC₅₀ higher than 6 μM. I as norepinephrine reuptake inhibitors should prove useful in the treatment of disorders that are associated with norepinephrine dysfunction. Pharmaceutical compns. comprising I are disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:248117 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 143:279
 TITLE: Cytochrome P450-dependent metabolism of gefitinib
 AUTHOR(S): Mckillop, D.; McCormick, A. D.; Millar, A.; Miles, G.
 S.; Phillips, P. J.; Hutchison, M.
 CORPORATE SOURCE: Drug Metabolism and Pharmacokinetics Department,
 AstraZeneca, Macclesfield, UK
 SOURCE: Xenobiotica (2005), 35(1), 39-50
 CODEN: XENOBH; ISSN: 0049-8254

PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro metabolism of [14C]-gefitinib (1-3 µM) was investigated using human liver microsomes and a range of expressed human cytochrome P 450 enzymes, with particular focus on the formation of O-desmethyl-gefitinib (M523595), the major metabolite observed in human plasma. High-performance liquid chromatog. with UV light, radiochem. and mass spectral anal., together with the availability of authentic stds., enabled quantification and structural identification of metabolites. On incubation with pooled human liver microsomes, [14C]-gefitinib underwent rapid and extensive metabolism to a number of metabolites, although M523595 was only a minor microsomal product. Formation of most metabolites was markedly decreased by ketoconazole, but M523595 production was inhibited only by quinidine. Gefitinib was metabolized extensively by expressed CYP3A4, producing a similar range of metabolites to liver microsomes, but M523595 was not formed. CYP1A2, 2C9 and 2C19 produced no measurable metabolism of gefitinib, while CYP3A5 produced a range of metabolites similar to CYP3A4, but to a much lower degree. In contrast, CYP2D6 catalyzed rapid and extensive metabolism of gefitinib to M523595. While formation of M523595 was CYP2D6 mediated, the overall metabolism of gefitinib was dependent primarily on CYP3A4, and this was not obviously diminished in liver microsomes from CYP2D6 poor metabolizers.

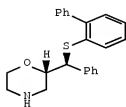
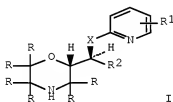
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L24 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:238982 CAPLUS Full-text
DOCUMENT NUMBER: 142:316847
TITLE: Preparation of homochiral pyridinylmorpholines
as selective norepinephrine reuptake
inhibitors
INVENTOR(S): Clark, Barry Peter; Gallagher, Peter Thaddeus
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005023802	A1	20050317	WO 2004-US22313	
20040809				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,			
CA, CH,	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,			
GB, GD,	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,			
KZ, LC,				

NA, NI, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
 SL, SY, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 ZM, ZW TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG
 EP 1658287 A1 20060524 EP 2004-778025
 20040809 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
 PRIORITY APPLN. INFO.: GB 2003-19693 A
 20030822 US 2003-514748P P
 20031027 WO 2004-US22313 W
 20040809
 OTHER SOURCE(S): CASREACT 142:316847; MARPAT 142:316847
 GI



AB Title compds. I [X = S, O; R = H, alkyl; R1 = H, alkyl, alkoxy,
 halo, etc.; R2 = alkyl, Ph, etc.] are prepared For instance, (S)-
 (4- benzylmorpholin-2-yl)phenylmethanone (large scale preparation
 given) is selectively reduced to the (S,S) alc. and converted to
 the corresponding thiol in 3 addnl. steps. The thiol is reacted
 with 2-fluoro-3-phenylpyridine and debenzylated to give II. All
 example compds. exhibit a Ki < 500 nM at the norepinephrine
 transporter and all examples of I inhibit selectively the
 norepinephrine transporter relative to serotonin and dopamine by
 at least a factor of 5. I are useful for the treatment of, e.g.,
 an addictive disorder, withdrawal syndrome, etc.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE
 FOR THIS

RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE

L24 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:902904 CAPLUS Full-text
 DOCUMENT NUMBER: 141:388319
 TITLE: Potent N-(1,3-Thiazol-2-yl)pyridin-2-amine
 Vascular Endothelial Growth Factor Receptor Tyrosine
 Kinase Inhibitors with Excellent Pharmacokinetics and
 Low Affinity for the hERG Ion Channel
 AUTHOR(S): Bilodeau, Mark T.; Balitza, Adrienne E.;
 Koester, Timothy J.; Manley, Peter J.; Rodman, Leonard
 D.; Buser-Doepner, Carolyn; Coll, Kathleen E.;
 Fernandes, Christine; Gibbs, Jackson B.; Heimbrook, David
 C.; Huckle, William R.; Kohl, Nancy; Lynch, Joseph
 J.; Mao, Xianzhi; McFall, Rosemary C.; McLoughlin,
 Debra; Miller-Stein, Cynthia M.; Rickert, Keith W.;
 Sepp-Lorenzino, Laura; Shipman, Jennifer M.;
 Subramanian, Raju; Thomas, Kenneth A.; Wong,
 Bradley K.; Yu, Sean; Hartman, George D.
 CORPORATE SOURCE: Departments of Medicinal Chemistry, Cancer
 Research, Drug Metabolism and Pharmacology, Merck
 Research Laboratories, West Point, PA, 19486, USA
 SOURCE: Journal of Medicinal Chemistry (2004), 47(25),
 6363-6372
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:388319
 AB A series of N-(1,3-thiazol-2-yl)pyridin-2-amine KDR kinase
 inhibitors have been developed that possess optimal properties.
 Comps. have been discovered that exhibit excellent in vivo
 potency. The particular challenges of overcoming hERG binding
 activity and QTc increases in vivo in addition to achieving good
 pharmacokinetics have been accomplished by discovering a unique
 class of amine substituents. These comps. have a favorable
 kinase selectivity profile that can be accentuated with
 appropriate substitution.
 REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L24 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:45136 CAPLUS Full-text
 DOCUMENT NUMBER: 136:81216

TITLE: Predicting the mutagenicity of tobacco-related N-nitrosamines in humans using 11 strains of *Salmonella typhimurium* YG7108, each coexpressing a form of human cytochrome P450 along with NADPH-cytochrome P450 reductase

AUTHOR(S): Fujita, Ken-Ichi; Kamataki, Tetsuya

CORPORATE SOURCE: Laboratory of Drug Metabolism, Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo, 060 0812, Japan

SOURCE: Environmental and Molecular Mutagenesis (2001), 38(4), 339-346

CODEN: EMMUEG; ISSN: 0893-6692

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tobacco, including snuff and chewing tobacco, contains N-nitrosamines such as 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), N-nitrosodiethylamine (NDEA), N-nitrosopyrrolidine (NPYR), N-nitrosopiperidine (NPIP), N-nitrosomorpholine (NMOR), N-nitrosornicotine (NNN), N-nitrosoanabasine (NABS), and N-nitrosoanatabine (NATB). The role of human cytochrome P 450 (CYP) in the metabolic activation of these tobacco-related N-nitrosamines was examined by a *Salmonella* mutation test using genetically engineered *Salmonella typhimurium* (S. typhimurium) YG7108 cells each expressing a form of human CYP (CYP1A1, CYP1A2, CYP1B1, CYP2A6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4, or CYP3A5) together with human NADPH-cytochrome P 450 reductase. Mutagen production from NNK was catalyzed by CYP in the following order: CYP1A2, CYP1A1, CYP1B1, CYP2A6, CYP2C19, CYP3A4. The metabolic activation of one of the N-alkylnitrosamines, NDEA, was mediated by CYP2A6, followed by CYP2E1. Cyclic N-nitrosamines such as NPYR, NPIP, and NMOR were also primarily activated by CYP2A6, and to a lesser extent by CYP2E1. NNN, a pyridine derivative of NPYR, was activated by CYP1A1 at an efficiency similar to that of CYP2A6. NABS, a pyridine derivative of NPIP, was mainly activated by CYP3A4, followed by CYP1A1 and CYP2A6. Thus, the addition of a pyridine ring to NPYR or NPIP altered the forms of CYP primarily responsible for mutagenic activation. NATB was metabolically activated solely by CYP2A6, whereas the genotoxicity of NATB was much lower than that of NNN or NPYR. Based on these data, we conclude that CYP2A6 was responsible for the mutagenic activation of essentially all tobacco-related N-nitrosamines tested in the present study.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:850925 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:581

TITLE: Antisense cytochrome P450 inhibitors for metabolic

INVENTOR(S): improvement of drug actions
 Iversen, Patrick L.
 PATENT ASSIGNEE(S): Avi Biopharma, Inc., USA
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087286	A2	20011122	WO 2001-US15857	
20010516				
WO 2001087286	A3	20030213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6686338	B1	20040203	US 2000-574570	
20000517				
US 6673778	B1	20040106	US 2000-737452	
20001213				
CA 2408746	A1	20011122	CA 2001-2408746	
20010516				
EP 1303596	A2	20030423	EP 2001-937461	
20010516				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004523465	T	20040805	JP 2001-583754	
20010516				
AU 2001263197	B2	20061109	AU 2001-263197	
20010516				
PRIORITY APPLN. INFO.:			US 2000-574570	A2
20000517			US 2000-737452	A2
20001213			US 1996-12219P	P
19960223			US 1997-802859	B2
19970219			WO 2001-US15857	W
20010516				

AB A method is described for improving the pharmacokinetics of a drug in a subject, by co-administering oligomers, preferably PMO's (phosphorodiamidate morpholine oligonucleotides), antisense to RNAs encoding drug-metabolizing enzymes, particularly P 450 enzymes. The oligomers reduce production of the drug-metabolizing enzymes, which extends drug half-life and effectiveness and/or decreases drug toxicity.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L24 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:419680 CAPLUS Full-text

DOCUMENT NUMBER: 133:114906

TITLE: Identification of cytochrome P450 isoform involved in

the metabolism of YM992, a novel selective serotonin

re-uptake inhibitor, in human liver microsomes
AUTHOR(S): Noguchi, K.; Mera, A.; Watanabe, T.; Higuchi,

S.; Chiba, K.

CORPORATE SOURCE: Drug Metabolism Laboratories, Yamanouchi
Pharmaceutical Co., Ltd., Tokyo, 174-8511,

Japan

SOURCE: Xenobiotica (2000), 30(5), 503-513

CODEN: XENOBH; ISSN: 0049-8254

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1. In vitro studies were conducted to identify the hepatic cytochrome P 450 isoform involved in the metabolism of YM992, ((S)-2-[[[(fluoro-4-indanyl)oxy]methyl]morpholine monohydrochloride), a novel serotonin re-uptake inhibitor, in human liver microsomes. 2. Microsomes prepared from yeast expressing CYP1A1, CYP1A2 and CYP2D6 effectively metabolized YM992. A significant correlation was observed between the rate of YM992 metabolism and 7-ethoxyresorufin O-deethylation, CYP1A1/2 specific activity, in liver microsomes from 16 individual donors ($r^2 = 0.628$, $p < 0.001$). α -Naphthoflavone and isosafrole, CYP1A1/2 inhibitors, suppressed the metabolism of YM992 in human liver microsomes in a concentration-dependent manner. 3. The metabolism of YM992 in human liver microsomes was inhibited by approx. 95% by antibodies which recognize both CYP1A1 and CYP1A2 whereas antibodies specific for CYP1A1 did not show inhibitory effects. 4. The same major metabolites, M6 and M7, were generated from YM992 after incubation with human liver microsomes and recombinant human CYP1A2. 5. These results suggest that the metabolism of YM992 in human liver microsomes is mainly catalyzed by CYP1A2, and that YM992 might increase plasma concentration of concomitant drugs metabolized by CYP1A2 due to competitive inhibition.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L24 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1998:241719 CAPLUS Full-text
 DOCUMENT NUMBER: 129:12257
 ORIGINAL REFERENCE NO.: 129:2510h,2511a
 TITLE: Overlapping substrate specificities of
 cytochrome P450 3A and P-glycoprotein for a novel cysteine
 protease inhibitor
 AUTHOR(S): Zhang, Yuanchao; Guo, Xisheng; Lin, Emil T.;
 Benet, Leslie Z.
 CORPORATE SOURCE: Department of Biopharmaceutical Sciences,
 School of Pharmacy, University of California, San
 Francisco, CA, 94143-0446, USA
 SOURCE: Drug Metabolism and Disposition (1998), 26(4),
 360-366
 CODEN: DMSDAI; ISSN: 0090-9556
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB K02 (morpholine-urea-Phe-Hphe-vinylsulfone), a newly developed
 peptidomimetic, acts as a potent cysteine protease inhibitor,
 especially of cathepsins B and L (which are associated with cancer
 progression) and cruzain (a cysteine protease of Trypanosoma
 cruzi, which is responsible for Chagas' disease). Here we
 investigated features of the disposition of K02 using in vitro
 systems, characterizing the interaction of the drug with human
 cytochrome P 450 (CYP) 3A and P-glycoprotein (P-gp), a mediator of
 multidrug resistance (MDR) to cancer chemotherapy and a counter-
 transporter in the intestine that limits oral drug
 bioavailability. P-gp functions as an ATP-dependent drug efflux
 pump to reduce intracellular cytotoxic concns. An HPLC assay was
 developed to analyze K02 and its metabolites formed in human liver
 microsomes. Three major primary metabolites were determined by
 LC/MS/MS to be hydroxylated products of the parent compound A
 rabbit anti-CYP3A polyclonal antibody (200 µl antibody/mg
 microsomal protein) produced 75-94% inhibition of the formation of
 these three hydroxylated metabolites. Ketoconazole (5 µM), a
 selective CYP3A inhibitor, produced up to 75% inhibition, whereas
 other CYP-specific inhibitors, i.e. quinidine (CYP2D6), 7,8-
 benzoflavone (CYP1A2), and sulfaphenazole (CYP2C9), showed no
 significant effects. An identical metabolite formation profile
 for K02 was observed with cDNA-expressed human CYP3A4 (Gentest).
 These data demonstrate that K02 is a substrate for CYP3A.
 Formation of 1'-hydroxymidazolam, the primary human midazolam
 metabolite, was markedly inhibited by K02 via competitive
 processes, which suggests the potential for drug-drug interactions
 of K02 with other CYP3A substrates. K02 significantly inhibited
 the photoaffinity labeling of P-gp with azidopine and LU-49888, a
 photoaffinity analog of verapamil. Transport studies with
 [14C]K02, using MDRL-transfected Madin-Darby canine kidney cell
 monolayers in the Transwell system, demonstrated that the
 basolateral-to-apical flux of K02 across MDRL-transfected Madin-

Darby canine kidney cells was markedly greater than the apical-to-basolateral flux (ratio of 63 with 10 μ M [14C]K02). This suggests that K02 is also a P-gp substrate. These studies are important for formulating strategies to increase the absorption and/or decrease the elimination of K02 and to optimize its delivery to malignant cells and parasite-infected host cells.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

<http://www.cas.org/support/stngen/stdoc/properties.html>

=> e atomoxetine/cn

E1	1	ATOMLINE 15 YELLOW/CN
E2	1	ATOMO DESINFLAMANTE/CN
E3	1	--> ATOMOXETINE/CN
E4	1	ATOMOXETINE (+)-MANDELATE/CN
E5	1	ATOMOXETINE (S)-(+)-MANDELATE/CN
E6	1	ATOMOXETINE (S)-MANDELATE/CN
E7	1	ATOMOXETINE HYDROCHLORIDE/CN
E8	1	ATOMSAFRON H/CN
E9	1	ATOMTHENE 30/CN
E10	1	ATOMU 8000/CN
E11	1	ATOMUORUMAITE/CN
E12	1	ATOMUSERA 300/CN

=> s e3

L26 1 ATOMOXETINE/CN

=> d l26

L26 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 83015-26-3 REGISTRY

ED Entered STN: 16 Nov 1984

CN Benzenepropanamine, N-methyl- γ -(2-methylphenoxy)-, (YR)- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzenepropanamine, N-methyl- γ -(2-methylphenoxy)-, (R)-

OTHER NAMES:

CN (-)-Tomoxetine

CN Atomoxetine

CN Tomoxetine

FS STEREOSEARCH

MF C17 H21 N O

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,

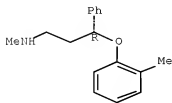
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RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

340 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
340 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> e reboxetine/cn

E1	1	REBOUL COCKTAIL/CN
E2	1	REBOUND/CN
E3	1	--> REBOXETINE/CN
E4	1	REBOXETINE FUMARATE/CN
E5	1	REBOXETINE HYDROBROMIDE/CN
E6	1	REBOXETINE MESILATE/CN
E7	1	REBOXETINE MESYLATE/CN
E8	1	REBOXITINE/CN
E9	1	REBRAMIN/CN
E10	1	REBREDOXIN (NEISSERIA LACTAMICA)/CN
E11	1	REBRIDEN/CN
E12	1	REBUILDA/CN

=> s e3

L27 1 REBOXETINE/CN

=> d l27

L27 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 71620-89-8 REGISTRY

ED Entered STN: 16 Nov 1984

CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel- (CA
INDEX

NAME)

OTHER NAMES:

CN Reboxetine

CN Reboxitine

FS STEREOSEARCH

DR 98769-81-4, 98769-83-6, 71621-36-8

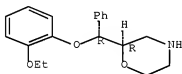
MF C19 H23 N O3

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,

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 BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM,
 DDFU,
 DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH,
 IPA,
 MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*,
 SYNTHLINE,
 TONCENTER, USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: WHO

Relative stereochemistry.



=> s 128 and (serotonin or ?epinephrin? or adrenerg? or mental?)
 76823 SEROTONIN
 53 SEROTONINS
 76828 SEROTONIN
 (SEROTONIN OR SEROTONINS)
 66723 ?EPINEPHRIN?
 78668 ADRENERG?
 66814 MENTAL?
 L30 70 L28 AND (SEROTONIN OR ?EPINEPHRIN? OR ADRENERG? OR
 MENTAL?)
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L31 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:931170 CAPLUS Full-text
 DOCUMENT NUMBER: 139:391377
 TITLE: Method using anticonvulsant agents and
 compounds enhancing norepinephrine and/or dopamine
 activity for treating obesity
 INVENTOR(S): Gadde, Kishore M.; Krishnan, K. Ranga R.
 PATENT ASSIGNEE(S): Duke University, USA
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003097046      A1      20031127      WO 2003-US15703
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LK, LR,
      LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
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      AU 2003231788      B2      20080911
      EP 1505967      A1      20050216      EP 2003-753096
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      CN 1652778      A      20050810      CN 2003-811229
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      CN 1320886      C      20070613
      JP 2005530782      T      20051013      JP 2004-505045
20030519 <--
      RU 2341259      C2      20081220      RU 2004-131636
20030519 <--
      MX 2004011203      A      20050714      MX 2004-11203
20041111 <--
      US 20080319036      A1      20081225      US 2008-205769
20080905 <--
PRIORITY APPLN. INFO.:      US 2002-380874P      P
20020517 <--
      US 2003-440404      A1
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      WO 2003-US15703      W
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      US 2004-830071      A1
20040423
OTHER SOURCE(S):      MARPAT 139:391377
AB      The invention provides a method for treating obesity and
minimizing metabolic risk factors associated therewith using e.g.
zonisamide or other weight loss-promoting anticonvulsants, either
alone or in combination with bupropion or other compound that

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enhances the activity of norepinephrine and/or dopamine via uptake inhibition or other mechanism.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L31 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:472376 CAPLUS Full-text
 DOCUMENT NUMBER: 139:30841
 TITLE: Use of norepinephrine reuptake inhibitors for the treatment of cognitive failure
 INVENTOR(S): Bymaster, Franklin Porter; Gehlert, Donald Richard;
 PATENT ASSIGNEE(S): McKinzie, David Lee; Yang, Charles Renkin Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003049724	A1	20030619	WO 2002-US36132	
20021127 <--				
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BR 2002013581	A	20040824	BR 2002-13581	
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EP 1458368	A1	20040922	EP 2002-789574	
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EP 1458368	B1	20071121		
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 HU 2004002619 A2 20050329 HU 2004-2619
 20021127 <--
 HU 2004002619 A3 20080428
 JP 2005517647 T 20050616 JP 2003-550773
 20021127 <--
 CN 1713900 A 20051228 CN 2002-824726
 20021127 <--
 NZ 532065 A 20070330 NZ 2002-532065
 20021127 <--
 ES 2295435 T3 20080416 ES 2002-789574
 20021127 <--
 US 20050009925 A1 20050113 US 2004-496765
 20040525 <--
 ZA 2004004274 A 20050913 ZA 2004-4274
 20040531 <--
 IN 2004KN00770 A 20060414 IN 2004-KN770
 20040607 <--
 MX 2004005716 A 20041206 MX 2004-5716
 20040611 <--
 NO 2004002904 A 20040907 NO 2004-2904
 20040709 <--
 PRIORITY APPLN. INFO.: US 2001-339174P P
 20011211 <-- WO 2002-US36132 W
 20021127 <--

OTHER SOURCE(S): MARPAT 139:30841

AB Selective norepinephrine reuptake inhibitors, particularly atomoxetine, reboxetine and 2-alkylthio substituted phenoxyphenyl propylamines, are used for the treatment of cognitive failure, including cognitive failure due to dementia, delirium and schizophrenia.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:454102 CAPLUS Full-text
 DOCUMENT NUMBER: 139:974
 TITLE: Use of norepinephrine reuptake inhibitors for the treatment of tic disorders
 INVENTOR(S): Allen, Albert John; Michelson, David
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 23 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047560	A1	20030612	WO 2002-US33628	
20021112 <--				
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CH, CN,
 GE, GH,
 LK, LR,
 OM, PH,
 TR, TT,
 TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY,
 EE, ES,
 BJ, CF,
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2466649 A1 20030612 CA 2002-2466649
 20021112 <--
 AU 2002347984 A1 20030617 AU 2002-347984
 20021112 <--
 EP 1455770 A1 20040915 EP 2002-784195
 20021112 <--
 EP 1455770 B1 20070620
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
 JP 2005515199 T 20050526 JP 2003-548816
 20021112 <--
 AT 365035 T 20070715 AT 2002-784195
 20021112 <--
 ES 2287338 T3 20071216 ES 2002-784195
 20021112 <--
 US 20050014843 A1 20050120 US 2004-495303
 20040511 <--
 US 20080200555 A1 20080821 US 2008-60318
 20080401 <--
 PRIORITY APPLN. INFO.: US 2001-334494P P
 20011130 <--
 WO 2002-US33628 W
 20021112 <--
 US 2004-495303 A1
 20040511
 OTHER SOURCE(S): MARPAT 139:974
 AB Selective norepinephrine reuptake inhibitors, e.g. atomoxetine,
 are used to treat tic disorders.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L31 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:878171 CAPLUS Full-text
 DOCUMENT NUMBER: 139:750
 TITLE: Atomoxetine increases extracellular levels of
 norepinephrine and dopamine in prefrontal
 cortex of rat: a potential mechanism for

efficacy in

AUTHOR(S):
David

Attention Deficit/Hyperactivity Disorder
Bymaster, Frank P.; Katner, Jason S.; Nelson,
L.; Hemrick-Luecke, Susan K.; Threlkeld, Penny
G.;
Heiligenstein, John H.; Morin, S. Michelle;

Gehlert,

Donald R.; Perry, Kenneth W.

CORPORATE SOURCE:

Neuroscience Research Division, Lilly Research
Laboratories, Indianapolis, IN, USA

SOURCE:

Neuropsychopharmacology (2002), 27(5),
699-711

CODEN: NEROEW; ISSN: 0893-133X

PUBLISHER:

Elsevier Science Inc.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The selective norepinephrine (NE) transporter inhibitor atomoxetine (formerly called tomozetine or LY139603) has been shown to alleviate symptoms in Attention Deficit/Hyperactivity Disorder (ADHD). We investigated the mechanism of action of atomoxetine in ADHD by evaluating the interaction of atomoxetine with monoamine transporters the effects on extracellular levels of monoamines, and the expression of the neuronal activity marker Fos in brain regions. Atomoxetine inhibited binding of radioligands to clonal cell lines transfected with human NE, serotonin (5-HT) and dopamine (DA) transporters with dissociation constants (K_d) values of 5, 77 and 1451 nM, respectively, demonstrating selectivity for NE transporters. In microdialysis studies, atomoxetine increased extracellular (EX) levels of NE in prefrontal cortex (PFC) 3-fold, but did not alter 5-HT levels. Atomoxetine also increased DAEX concns. in PFC 3-fold, but did not alter DAEX in striatum or nucleus accumbens. In contrast, the psychostimulant methylphenidate, which is used in ADHD therapy, increased NEEX and DAEX equally in PFC, but also increased DAEX in the striatum and nucleus accumbens to the same level. The expression of the neuronal activity marker Fos was increased 3.7-fold in PFC by atomoxetine administration, but was not increased in the striatum or nucleus accumbens, consistent with the regional distribution of increased DAEX. We hypothesize that the atomoxetine-induced increase of catecholamines in PFC, a region involved in attention and memory, mediates the therapeutic effects of atomoxetine in ADHD. In contrast to methylphenidate, atomoxetine did not increase DA in striatum or nucleus accumbens, suggesting it would not have motoric or drug abuse liabilities.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L31 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:

2002:777652 CAPLUS [Full-text](#)

DOCUMENT NUMBER:

137:273226

TITLE:

Acute pharmacologic augmentation of

psychotherapy with

enhancers of learning or conditioning

INVENTOR(S):

Davis, Michael; Lu, Kwok-Tung; Ressler, Kerry

J.
 PATENT ASSIGNEE(S): Emory University, USA
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078629	A2	20021010	WO 2002-US9467	
20020328 <--				
WO 2002078629	A3	20021128		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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CA 2442330	A1	20021010	CA 2002-2442330	
20020328 <--				
AU 2002311784	A1	20021015	AU 2002-311784	
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AU 2002311784	B2	20071122		
EP 1383465	A2	20040128	EP 2002-739111	
20020328 <--				
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JP 2004530666	T	20041007	JP 2002-576897	
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US 20040208923	A1	20041021	US 2004-473640	
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US 20050096396	A1	20050505	US 2004-924591	
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US 20060252761	A1	20061109	US 2006-347937	
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20020313 <--				
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			US 2003-492795P	P

20030806 US 2003-533003P P
 20031229 US 2004-473640 A2
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 20040803 US 2004-924591 A2
 20040824 US 2004-625253P P
 20041105 US 2004-24921 A2
 20041229 US 2005-651114P P
 20050208 US 2005-667140P P
 20050331

AB Methods for treating an individual with a psychiatric order with a pharmacol. agent that enhances learning or conditioning in combination with a session of psychotherapy are provided. These methods of the invention encompass a variety of methods of psychotherapy, and psychodynamically oriented psychotherapy, and psychiatric orders including fear and anxiety disorders, addictive disorders, addictive disorders including substance-abuse disorders, and mood disorders. The pharmacol. agents used for the methods of the present invention are ones that generally enhance learning or conditioning, including those that increase the level of norepinephrine in the brain, those that increase the level of acetylcholine in the brain, and those that enhance N-methyl-D-aspartate (NMDA) receptor transmission in the brain.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2009 ACS on SIN
 ACCESSION NUMBER: 2002:521465 CAPLUS Full-text
 DOCUMENT NUMBER: 137:98994
 TITLE: Pharmaceuticals containing a combination of norepinephrine reuptake inhibitors and neuroleptics
 INVENTOR(S): Wong, Erik Ho Fong; Gallen, Christopher C.; Svensson,
 Torngy
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA; Pharmacia AB
 SOURCE: PCT Int. Appl., 22 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053140	A2	20020711	WO 2001-US45871	

20011227 <--

WO 2002053140 A3 20021024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2431041 A1 20020711 CA 2001-2431041
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AU 2002232470 A1 20020716 AU 2002-232470
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AU 2002232470 B2 20051103
EP 1353675 A2 20031022 EP 2001-991997
20011227 <--
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JP 2004517112 T 20040610 JP 2002-554091
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NZ 526801 A 20050729 NZ 2001-526801
20011227 <--
US 20020156067 A1 20021024 US 2001-35100
20011228 <--
US 6964962 B2 20051115
MX 2003006003 A 20050908 MX 2003-6003
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US 20060003992 A1 20060105 US 2005-219901
20050906 <--
PRIORITY APPLN. INFO.: US 2001-259286P P
20010102 <--
WO 2001-US45871 W
20011227 <--
US 2001-35100 A3
20011228 <--

AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a salt; and (b) 1 or more neuroleptics is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating schizophrenia. A pharmaceutical composition was prepared by combining reboxetine with a neuroleptic in an acceptable carrier. The composition contains 0.01-10 mg reboxetine and 25-300 mg clozapine.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:391520 CAPLUS Full-text
 DOCUMENT NUMBER: 136:363874
 TITLE: Selective norepinephrine reuptake inhibitors
 for the treatment of anxiety disorders
 INVENTOR(S): Thomasson, Holly Read; Michelson, David
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 20 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040006	A2	20020523	WO 2001-US27801	
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WO 2002040006	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2426069	A1	20020523	CA 2001-2426069	
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AU 2002017757	A	20020527	AU 2002-17757	
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HU 2003001863	A2	20030929	HU 2003-1863	
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EP 1395253	A2	20040310	EP 2001-996376	
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JP 2004529073	T	20040924	JP 2002-542380	
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BR 2001015301	A	20041214	BR 2001-15301	
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CN 1822825	A	20060823	CN 2001-818927	
20011106 <--				
US 20040034106	A1	20040219	US 2003-416294	

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 IN 2003KN00601 A 20050121 IN 2003-KN601
 20030512 <--
 NO 2003002156 A 20030513 NO 2003-2156
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 MX 2003004190 A 20030922 MX 2003-4190
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 HR 2003000384 A1 20030831 HR 2003-384
 20030514 <--
 ZA 2003003738 A 20040826 ZA 2003-3738
 20030514 <--
 PRIORITY APPLN. INFO.: US 2000-249010P P
 20001115 <--
 US 2001-265362P P
 20010131 <--
 WO 2001-US27801 W
 20011106 <--
 OTHER SOURCE(S): MARPAT 136:363874
 AB Selective norepinephrine reuptake inhibitors, e.g. tomoxetine, are
 used to treat anxiety disorders, especially obsessive-compulsive
 disorder.
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L31 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:676591 CAPLUS Full-text
 DOCUMENT NUMBER: 135:216029
 TITLE: Treatment of psoriasis with norepinephrine
 reuptake inhibitors
 INVENTOR(S): Thomasson, Holly Read
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066101	A2	20010913	WO 2001-US5260	
20010220 <--				
WO 2001066101	A3	20020207		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,				
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GM, HR,				
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
LS, LT,				
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,				
RO, RU,				
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,				
UZ, VN,				
YU, ZA, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
 CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2400571 A1 20010913 CA 2001-2400571
 20010220 <--
 EP 1267859 A2 20030102 EP 2001-918185
 20010220 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 BR 2001008980 A 20030603 BR 2001-8980
 20010220 <--
 HU 2002004551 A2 20030628 HU 2002-4551
 20010220 <--
 JP 2003525899 T 20030902 JP 2001-564754
 20010220 <--
 IN 2002KN00846 A 20050311 IN 2002-KN846
 20020624 <--
 ZA 2002005266 A 20031001 ZA 2002-5266
 20020701 <--
 US 20030045585 A1 20030306 US 2002-203403
 20020807 <--
 US 6683114 B2 20040127
 MX 2002008659 A 20030224 MX 2002-8659
 20020904 <--
 NO 2002004236 A 20020905 NO 2002-4236
 20020905 <--
 PRIORITY APPLN. INFO.: US 2000-187508P P
 20000307 <--
 WO 2001-US5260 W
 20010220 <--
 OTHER SOURCE(S): MARPAT 135:216029
 AB Norepinephrine reuptake inhibitors, e.g., tomoxetine or its salts,
 reboxetine, duloxetine, are used to treat psoriasis. Thus, hard
 gelatin capsules contained tomoxetine-HCl 30.0, starch 305.0, and
 Mg stearate 5.0 mg/capsule.

L31 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:635946 CAPLUS Full-text
 DOCUMENT NUMBER: 135:190433
 TITLE: Therapeutic agents for treating obesity
 INVENTOR(S): Heal, David John; Cheetham, Sharon Crawford
 PATENT ASSIGNEE(S): Knoll Aktiengesellschaft, Germany
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001062341	A2	20010830	WO 2001-EP1894	

20010220 <--
 WO 2001062341 A3 20020131
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2400797 A1 20010830 CA 2001-2400797
 20010220 <--
 AU 2001052135 A 20010903 AU 2001-52135
 20010220 <--
 EP 1259292 A2 20021127 EP 2001-925343
 20010220 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2003523410 T 20030805 JP 2001-561399
 20010220 <--
 US 20030130355 A1 20030710 US 2002-204392
 20021112 <--
 PRIORITY APPLN. INFO.: GB 2000-4003 A
 20000222 <--
 WO 2001-EP1894 W
 20010220 <--
 AB The present invention provides a method of treating and preventing obesity and related co-morbid conditions comprising the administration of a therapeutically effective amount of one or more monoamine reuptake inhibitors which are serotonin reuptake inhibitors and/or noradrenaline reuptake inhibitors and a 5-HT1A agonist to a patient in need thereof. Monoamine reuptake inhibitors such as sibutramine are useful in treating obesity but have cardiovascular side-effects which can be diminished by administration of a 5-HT1A agonist such as flesinoxan. An example is given in which flesinoxan reduces the cardiovascular (blood pressure, heart rate) effects of sibutramine in rats.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE
 L31 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:635879 CAPLUS Full-text
 DOCUMENT NUMBER: 135:200472
 TITLE: Norepinephrine reuptake inhibitor and antimuscarinic agent combinations
 INVENTOR(S): Rogosky, Karen; Jorn, Deborah

PATENT ASSIGNEE(S): Pharmacia & Upjohn Co., USA
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062236	A2	20010830	WO 2001-US3698	
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WO 2001062236	A3	20020307		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1257277	A2	20021120	EP 2001-910421	
20010123 <--				
EP 1257277	B1	20050615		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523382	T	20030805	JP 2001-561303	
20010123 <--				
NZ 520975	A	20040326	NZ 2001-520975	
20010123 <--				
CN 1660435	A	20050831	CN 2005-10003943	
20010123 <--				
PT 1257277	T	20050930	PT 2001-910421	
20010123 <--				
CA 2399442	A1	20010830	CA 2001-2399442	
20010223 <--				
AU 2001038028	A	20010903	AU 2001-38028	
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AU 781254	B2	20050512		
US 20020010216	A1	20020124	US 2001-792718	
20010223 <--				
AT 297735	T	20050715	AT 2001-910421	
20010223 <--				
ES 2241802	T3	20051101	ES 2001-910421	
20010223 <--				
MX 2002008183	A	20021129	MX 2002-8183	
20020822 <--				

PRIORITY APPLN. INFO.: US 2000-184790P P
20000224 <--

20010123 <-- CN 2001-804031 A3

20010123 <-- WO 2001-US3698 W

AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a pharmaceutically effective salt thereof; and (b) a pharmaceutically effective amount of one or more antimuscarinic agents or a pharmaceutically effective salt thereof is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating incontinence. A composition was prepared containing reboxetine in either its racemic or (S,S) enantiomer forms with tolterodine.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:282100 CAPLUS Full-text
DOCUMENT NUMBER: 130:316651
TITLE: Synergistic pharmaceutical compositions containing

INVENTOR(S): moxonidine
Perry, Kenneth Wayne
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9920279	A1	19990429	WO 1998-US21418	
19981009 <--				
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH,				
GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,				
LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI,				
SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA,				
GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306233	A1	19990429	CA 1998-2306233	
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AU 9896928	A	19990510	AU 1998-96928	
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EP 919234	A2	19990602	EP 1998-308225	
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EP 919234	A3	19990825		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
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ZA 9809251 A 20000410 ZA 1998-9251
19981009 <--
US 6066643 A 20000523 US 1998-169369
19981009 <--
JP 2001520195 T 20011030 JP 2000-516676
19981009 <--
PRIORITY APPLN. INFO.: US 1997-62282P P
19971017 <--
WO 1998-US21418 W

19981009 <--
AB A method for producing a potentiating effect on a therapeutic action of an agent which is selected from a serotonin re-uptake inhibitor, a norepinephrine re-uptake inhibitors, both a serotonin and norepinephrine re-uptake inhibitor, and an atypical antidepressant in a warm blooded mammal, comprises administering to said mammal an effective amount of moxonidine, or a pharmaceutically acceptable salt thereof. A tablet contained moxonidine 0.300, lactose 95.700, povidone 0.700, crospovidone 3.000, magnesium stearate 0.300, hydroxypropyl Me cellulose 1.300, Et cellulose 1.200, PEG 0.250, talc 0.975, red ferric oxide 0.025, and titanium dioxide 1.250 mg. Moxonidine at 0.2 mg twice daily when combined with 20 mg fluoxetine daily had synergistic effects in patients suffering major depression.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L31 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:231508 CAPLUS Full-text
DOCUMENT NUMBER: 130:262137
TITLE: Norepinephrine reuptake inhibitor for
treatment of oppositional defiant disorder
INVENTOR(S): Heiligenstein, John Harrison
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9915176	A1	19990401	WO 1998-US18114	
19980901 <--				
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CM, GA,

GN, GW, ML, MR, NE, SN, TD, TG
CA 2304115 A1 19990401 CA 1998-2304115
19980901 <--
AU 9891282 A 19990412 AU 1998-91282
19980901 <--
AU 740109 B2 20011101
BR 9812357 A 20000912 BR 1998-12357
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TR 200000755 T2 20000921 TR 2000-755
19980901 <--
JP 2001517627 T 20011009 JP 2000-512545
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HU 2000003591 A2 20020128 HU 2000-3591
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HU 2000003591 A3 20020228
NZ 502810 A 20020301 NZ 1998-502810
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CN 1146412 C 20040421 CN 1998-809196
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US 6028070 A 20000222 US 1998-156289
19980917 <--
EP 919236 A1 19990602 EP 1998-307650
19980921 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
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IE, SI, LT, LV, FI, RO
NO 2000001458 A 20000321 NO 2000-1458
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MX 2000002837 A 20010131 MX 2000-2837
20000322 <--
PRIORITY APPLN. INFO.: US 1997-59629P P
19970923 <-- WO 1998-US18114 W

19980901 <--
OTHER SOURCE(S): MARPAT 130:262137
AB Norepinephrine reuptake inhibitors (e.g. duloxetine) are used to
treat oppositional defiant disorder.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L31 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:231496 CAPLUS Full-text
DOCUMENT NUMBER: 130:262136
TITLE: Norepinephrine reuptake inhibitors for
treatment of conduct disorder
Heiligenstein, John Harrison
INVENTOR(S): Eli Lilly and Company, USA
PATENT ASSIGNEE(S): PCT Int. Appl., 18 pp.
SOURCE: CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9915163	A1	19990401	WO 1998-US18103	
19980901 <--				
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304657	A1	19990401	CA 1998-2304657	
19980901 <--				
CA 2304657	C	20051025		
AU 9890417	A	19990412	AU 1998-90417	
19980901 <--				
AU 740192	B2	20011101		
BR 9812371	A	20000919	BR 1998-12371	
19980901 <--				
TR 200000756	T2	20000921	TR 2000-756	
19980901 <--				
JP 2001517619	T	20011009	JP 2000-512532	
19980901 <--				
HU 2000004025	A2	20020128	HU 2000-4025	
19980901 <--				
HU 2000004025	A3	20020228		
NZ 502853	A	20020828	NZ 1998-502853	
19980901 <--				
CN 1762338	A	20060426	CN 2005-10099557	
19980901 <--				
US 6184222	B1	20010206	US 1998-156285	
19980917 <--				
EP 919235	A1	19990602	EP 1998-307630	
19980921 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2000001479	A	20000322	NO 2000-1479	
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MX 2000002829	A	20010131	MX 2000-2829	
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PRIORITY APPLN. INFO.:			US 1997-59628P	P
19970923 <--				
19980901 <--			CN 1998-809440	A3
19980901 <--			WO 1998-US18103	W
OTHER SOURCE(S):		MARPAT 130:262136		
AB		Norepinephrine reuptake inhibitors (e.g. duloxetine) are used to treat conduct disorder.		
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS		

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L31 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1997:545611 CAPLUS Full-text
 DOCUMENT NUMBER: 127:199618
 ORIGINAL REFERENCE NO.: 127:38543a
 TITLE: A stereoselective pharmacophoric model of the
 serotonin re-uptake site
 AUTHOR(S): Gundertofte, Klaus; Bogeso, Klaus P.;
 Liljefors, Tommy
 CORPORATE SOURCE: Research and Development, Copenhagen, DK-2500,
 Den.
 SOURCE: Computer-Assisted Lead Finding and
 Optimization:
 Current Tools for Medicinal Chemistry,
 [European
 Symposium on Quantitative Structure-Activity
 Relationships], 11th, Lausanne, Sept. 1-6,
 1996 (
 1997), Meeting Date 1996, 445-459. Editor(s):
 Van de Waterbeemd, Han; Testa, Bernard;
 Folkers, Gerd.
 Verlag Helvetica Chimica Acta: Basel, Switz.
 CODEN: 64VEAH
 CONFERENCE
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 AB Exhaustive conformational analyses on four selective serotonin
 reuptake inhibitors resulted in a pharmacophoric model explaining
 observed differences in enantioselectivities. A number of test
 compds. from a diverse set of chemical structures was included in
 the evaluation of the model. Furthermore, selectivity towards
 noradrenaline reuptake is explained.

=> file registry

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	ENTRY	SESSION
FULL ESTIMATED COST	89.92	1170.25
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-18.04	-33.62

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 DICTIONARY FILE UPDATES: 8 FEB 2009 HIGHEST RN 1102960-71-3

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Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document.

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      ('FLASH' OR 'FLASHES')
    1072 'HOT FLASH?'
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    492593 'HOT'
      52 'HOTS'
    492641 'HOT'
      ('HOT' OR 'HOTS')
    7436 'FLUSH'
    1240 'FLUSHES'
    8442 'FLUSH'
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    553 'HOT FLUSH?'
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    66729 ?EPINEPHRIN?
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    3972587 PRY<2003
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L2      13 L1 AND (PY<2003 OR PRY<2003 OR AY<2003)

=> d l2 ibib abs 1-13

L2 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:369266 CAPLUS Full-text
DOCUMENT NUMBER: 142:404276
TITLE: Method using adrenergic  $\alpha 2$ B antagonists, alone
or in combination with norepinephrine
reuptake inhibitors or dual norepinephrine
/serotonin reuptake inhibitors for treating
vasomotor
symptoms
INVENTOR(S): Deecher, Darlene Coleman; Beyer, Chad Edward;
Leventhal, Liza
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
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DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037260	A2	20050428	WO 2004-US33754	
20041013				
WO 2005037260	A3	20070816		
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US 20040152710	A1	20040805	US 2003-685812	
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JP 2007515395	T	20070614	JP 2006-535623
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EP 1846105	A2	20071024	EP 2004-794977
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			US 2002-418591P P
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			WO 2004-US33754 W
20041013			

AB The invention discloses selective adrenergic $\alpha 2B$ antagonists alone, selective adrenergic $\alpha 2B$ antagonists in combination with norepinephrine reuptake inhibitors (NRI) (as a single compound or as a combination of two or more compds.), or selective adrenergic $\alpha 2B$ antagonists in combination with dual norepinephrine reuptake inhibitors/serotonin reuptake inhibitors (NRI/SRI) (as a single compound or as a combination of two or more compds.) and methods of their use in the treatment of vasomotor symptoms.

L2 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:428915 CAPLUS Full-text

DOCUMENT NUMBER: 141:7039

TITLE: Propanamine derivatives, particularly 3-aryl-3-heteroaryloxy-1-propanamine

derivatives,

useful as serotonin and norepinephrine reuptake inhibitors, and their preparation, pharmaceutical compositions, and use,

particularly in

the treatment of pain

INVENTOR(S): Boulet, Serge Louis; Filla, Sandra Ann; Gallagher,

Peter Thaddeus; Hudziak, Kevin John;

Johansson, Anette

John

Michael;

Wolfe,

PATENT ASSIGNEE(S):

SOURCE:

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

Margareta; Karanjawala, Rushad E.; Masters,

Joseph; Matassa, Victor; Mathes, Brian

Rathmell, Richard Edmund; Whatton, Maria Ann;

Chad Nolan

Eli Lilly and Company, USA

PCT Int. Appl., 88 pp.

CODEN: PIXXD2

Patent

English

1

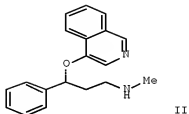
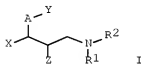
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AT 343566	T	20061115	AT 2003-777542		
20031024 <--					
ES 2274286	T3	20070516	ES 2003-777542		
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US 20060058360	A1	20060316	US 2005-532765		
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US 7410982	B2	20080812			
PRIORITY APPLN. INFO.:			US 2002-424126P		P
20021105 <--					

20031024

OTHER SOURCE(S):

MARPAT 141:7039

GI



AB New heteroaryloxy/thio 3-substituted propanamine compds I are provided [wherein: A = O or S; X = Ph (optionally substituted with up to 5 substituents each independently selected from halo, C1-4 alkyl, and C1-4 alkoxy), thienyl (optionally substituted with up to 3 substituents each independently selected from halo and C1-4 alkyl), and C2-8 alkyl, C2-8 alkenyl, C3-8 cycloalkyl and C4-8 cycloalkylalkyl (each of which may be optionally substituted with up to 3 substituents, each independently selected from halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkyl-S(O)n- (where n = 0, 1 or 2), CF3, CN and CONH2); Y = dihydrobenzothienyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, naphthylridyl, and thienopyridyl (each optionally substituted with up to 4 or 5 substituents each independently selected from halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkyl-S(O)n- (where n is 0, 1 or 2), nitro, acetyl, CF3, SCF3 and cyano); Z = H, OR3 or F; R3 = H, C1-6 alkyl, or phenyl-C1-6-alkyl; R1, R2 = independently H or C1-4 alkyl; and pharmaceutically acceptable salts thereof]. The compds. are useful as selective inhibitors of the reuptake of both serotonin and norepinephrine (no data). Use of I in the treatment of depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flushes/flushes, and pain, is claimed. Examples include 22 preps. of I, and addnl. preps. of numerous intermediates. For instance, Mitsunobu-type coupling of (S)-(-)-3-chloro-1-phenyl-1-propanol with isoquinolin-4-ol using a phosphonium reagent [155632-33-0] (47%), and aminolysis of the chloride product with aqueous MeNH2 in 1,4-dioxane in a sealed tube at 110° (80%), gave invention compound II, isolated as the mono-HCl salt after acidification with NH4Cl in MeOH.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE

L2 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:428895 CAPLUS Full-text

DOCUMENT NUMBER: 140:423467
 TITLE: Preparation of 3-aryloxy/thio-2,3-substituted
 propanamines and their use in inhibiting
 serotonin and
 norpinephrine reuptake
 INVENTOR(S): Boulet, Serge Louis; Filla, Sandra Ann;
 Gallagher, Peter Thaddeus; Hudziak, Kevin John;
 Johansson, Anette Margareta; Karanjawala, Rushad E.; Masters,
 John Joseph; Matassa, Victor; Mathes, Brian
 Michael; Rathmell, Richard Edmund; Whatton, Maria Ann;
 Wolfe, Chad Nolan
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 111 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043904	A1	20040527	WO 2003-US31514	
20031024 <--				
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EP 1587782	A1	20051026	EP 2003-777544	
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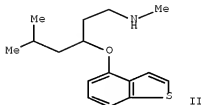
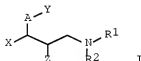
US 7417064
PRIORITY APPLN. INFO.:
20021105 <--

B2 20080826

US 2002-424117P P
WO 2003-US31514 W

20031024
OTHER SOURCE(S):
GI

MARPAT 140:423467



AB Title compds. I [A = O, S; X = (un)substituted Ph, thienyl; Y = Ph, naphthyl, dihydrobenzothienyl, benzothiazolyl, benzoisothiazolyl, quinolyl, etc.; Z = alkoxy, F; R1-2 = H, alkyl] are prepared For instance, 1-(benzylmethylamino)-5-methylhexan-3-ol (preparation given) is coupled to 4-hydroxybenzothiophene (PhMe, 1,1'-(azodicarbonyl)dipiperidine, Bu3P, 70°, 18 h) and the product debenzylated (1,2-dichloroethane, 1-chloroethyl chloroformate, reflux, 30 min) to give II. All example compds. have Ki < 100 nM at the serotonin transporter and norepinephrine transporter. I are useful for the treatment of, e.g., depression, OCD, anxiety and pain.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE

L2 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:428894 CAPLUS Full-text
DOCUMENT NUMBER: 140:423466
TITLE: Preparation of 3-aryloxy/thio-2,3-substituted propanamines and their use in inhibiting

serotonin and

norepinephrine reuptake

INVENTOR(S): Boulet, Serge Louis; Filla, Sandra Ann; Gallagher,

Peter Thaddeus; Hudziak, Kevin John;

Johansson, Anette

Margareta; Karanjawala, Rushad E.; Masters,

John

Joseph; Matassa, Victor; Mathes, Brian

Michael;

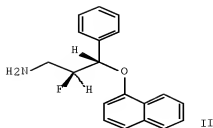
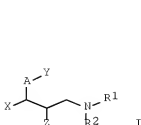
Rathmell, Richard Edmund; Whatton, Maria Ann;

Wolfe,

Chad Nolan

PATENT ASSIGNEE(S): Eli Lilly and Company, USA
 SOURCE: PCT Int. Appl., 164 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004043903	A1	20040527	WO 2003-US31513	
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OTHER SOURCE(S):	MARPAT 140:423466			
GI				



AB Title compds. I [A = O, S; X = (un)substituted Ph, thienyl; Y = Ph, naphthyl, dihydrobenzothienyl, benzothiazolyl, benzoisothiazolyl, quinolyl, etc.; Z = alkoxy, F; R1-2 = H, alkyl] are prepared For instance, (2R,3R)-3-phenylglycidol is treated with 1-naphthol (THF/H2O, NaOH, 75°, 4 h) to give (2R,3S)-3-(naphthalen-1-yloxy)-3-phenylpropane- 1,2-diol. This intermediate is converted to the mesylate (CH2Cl2, pyridine, 10°, MsCl), treated with NaN3 (DMF, 65°, 5 h), fluorinated (CH2Cl2, DMAP, DeOxo-Fluor) and reduced (THF, PPh3) to give II. All example compds. have Ki < 100 nM at the serotonin transporter and norepinephrine transporter. I are useful for the treatment of, e.g., depression, OCD, anxiety and pain.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L2 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:354797 CAPLUS Full-text
 DOCUMENT NUMBER: 140:350606
 TITLE: Use of norepinephrine reuptake modulators for preventing and treating vasomotor symptoms
 INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan
 Joseph; Leventhal, Liza; Sipe, Kimberly Jean; O'Connor, Lawrence Thomas
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
 SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035058	A1	20040429	WO 2003-US32759	

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BR 2004015280 A 20061219 BR 2004-15280
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CN 101189043 A 20080528 CN 2004-80037065
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PRIORITY APPLN. INFO.: US 2002-418591P P
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US 2003-685812 A
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US 2003-510897P P
20031014
WO 2003-US32759 W
20031015
US 2004-962897 A
20041012
WO 2004-US33754 W
20041013

AB The invention discloses the use of compds. and composition of
compds. that modulate norepinephrine levels for the prevention and
treatment of vasomotor symptoms, such as hot flush, caused by,
inter alia, thermoregulatory dysfunctions. Compds. of the
invention include e.g. desipramine.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L2 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:354778 CAPLUS Full-text
DOCUMENT NUMBER: 140:350603
TITLE: A method of treating vasomotor symptoms using
a

compound having norepinephrine reuptake
inhibitor activity and 5-HT2a antagonistic

activity

INVENTOR(S):

Deecker, Darlene Coleman; Merchenthaler,

Istvan Joseph

PATENT ASSIGNEE(S):

Wyeth, John, and Brother Ltd., USA

SOURCE:

PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035036	A1	20040429	WO 2003-US32554	
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US 20040180879	A1	20040916	US 2003-685974	
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CA 2502027	A1	20040429	CA 2003-2502027	
20031015 <--				
AU 2003282830	A1	20040504	AU 2003-282830	
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EP 1551380	A1	20050713	EP 2003-774828	
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BR 2003015346	A	20050823	BR 2003-15346	
20031015 <--				
CN 1705475	A	20051207	CN 2003-80101558	
20031015 <--				
JP 2006516023	T	20060615	JP 2004-545270	
20031015 <--				
MX 2005003980	A	20050803	MX 2005-3980	
20050414 <--				
PRIORITY APPLN. INFO.:			US 2002-418516P	P
20021015 <--				
			US 2003-685974	A
20031014				
			WO 2003-US32554	W
20031015				
AB	The invention discloses the use of compds. and compns. of compds. that modulate norepinephrine levels for the treatment of vasomotor symptoms, e.g. thermoregulatory disorders. The invention also discloses the use of compds. and compns. of compds. having			

norepinephrine reuptake inhibitor (NRI) activity alone or
 norepinephrine reuptake inhibitor and serotonin reuptake inhibitor
 (NRI/SRI) dual activity in combination with 5-HT2a receptor
 antagonist activity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L2 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:354777 CAPLUS Full-text

DOCUMENT NUMBER: 140:350602

TITLE: Use of norepinephrine reuptake modulators
 for preventing and treating vasomotor symptoms

INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler,
 Istvan

Joseph; Leventhal, Liza; Sipe, Kimberly Jean;
 O'Connor, Lawrence Thomas

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004035035	A1	20040429	WO 2003-US32760	
20031015 <--				
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GD, GE,				
			GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,	
LC, LK,				
			LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI,	
NO, NZ,				
			OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,	
TJ, TM,				
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			RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,	
AZ, BY,				
			KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,	
EE, ES,				
			FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI,	
SK, TR,				
			BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,	
TD, TG				
US 20040143008	A1	20040722	US 2003-684777	
20031014 <--				
US 7345096	B2	20080318		
CA 2502021	A1	20040429	CA 2003-2502021	
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AU 2003282862	A1	20040504	AU 2003-282862	
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EP 1551379 A1 20050713 EP 2003-774854
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 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003015314 A 20050816 BR 2003-15314
 20031015 <--
 CN 1705474 A 20051207 CN 2003-80101522
 20031015 <--
 JP 2006516243 T 20060629 JP 2004-545350
 20031015 <--
 MX 2005003982 A 20050803 MX 2005-3982
 20050414 <--
 US 20080227850 A1 20080918 US 2008-17232
 20080121 <--
 PRIORITY APPLN. INFO.: US 2002-418591P P
 20021015 <--
 US 2003-684777 A
 20031014
 WO 2003-US32760 W
 20031015

AB The invention discloses the use of compds. and compns. of compds.
 that modulate norepinephrine levels for the prevention and
 treatment of vasomotor symptoms, e.g. hot flush, caused by, inter
 alia, thermoregulatory dysfunctions. Compds. of the invention
 include e.g. venlafaxine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L2 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:776775 CAPLUS Full-text
 DOCUMENT NUMBER: 136:48623
 TITLE: Estrogen improves impaired musculoskeletal
 vascular
 adrenergic reactivity in pharmacologically
 ovariectomized rats: A potential peripheral
 mechanism
 for hot flashes?
 AUTHOR(S): Acs, N.; Vajo, Z.; Demendi, C.; Nadasy, G.;
 Monos, E.;
 Szekacs, B.
 CORPORATE SOURCE: Second Department of Obstetrics and
 Gynecology,
 Semmelweis University, Budapest, Hung.
 SOURCE: Gynecological Endocrinology (2001), 15(1),
 68-73
 CODEN: GYENER; ISSN: 0951-3590
 PUBLISHER: Parthenon Publishing Group Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Hot flashes are among the most common complaints of perimenopausal
 women. Despite the high prevalence of the phenomenon, the
 background to the development of hot flashes is still not
 completely understood, through a hypothesized central mechanism,
 involving norepinephrine and LH-releasing hormone (LH-RH)

secretion is widely accepted. The authors studied the influence of sex steroid deficiency and hormone replacement therapy on the biomech. properties of musculosutaneous arterioles, to see whether a peripheral mechanism also exists in the development of hot flashes. Fifty adult, nulliparous, non-pregnant female Sprague-Dawley rats received pharmacol. ovariectomy, and estradiol, medroxyprogesterone, or both hormones. After 12 wk the saphenous artery was isolated by microdissection. Norepinephrine-induced tone (active tangential strain) was measured as a function of intraluminal pressure in an organ bath. The norepinephrine-induced arterial tone was significantly different between the control group and the ovariectomized animals in the range of 80-150 mmHg intraluminal pressure. Also, significant differences were found between the ovariectomized group and the animals receiving estradiol monotherapy (between 80 and 170 mmHg, and between 180 and 200 mmHg intraluminal pressure). Neither medroxyprogesterone monotherapy nor combined hormone replacement therapy induced significant changes in the norepinephrine-induced vascular tone. The absence of sex steroids leads to decreased reactivity to norepinephrine in small musculosutaneous arteries, while chronic estradiol replacement therapy restores the impaired responsiveness of the vessels. The authors' data raise the possibility that in addition to the central mechanism, a previously unknown peripheral background mechanism for perimenopausal hot flashes may exist.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:753490 CAPLUS Full-text

DOCUMENT NUMBER: 134:275625

TITLE: Reboxetine in a neuroendocrine challenge

paradigm: evidence for high cortisol responses in healthy

volunteers scoring high on subclinical

depression

AUTHOR(S): Hennig, Juergen; Lange, Natalie; Haag, Anja; Rohrmann,

Sonja; Netter, Petra

CORPORATE SOURCE: Center for Psychobiology and Behavioral Medicine,

Department of Psychology, University of Giessen,

Giessen, D-35394, Germany

SOURCE: International Journal of Neuropsychopharmacology (

2000), 3(3), 193-201

CODEN: IJNUFB; ISSN: 1461-1457

PUBLISHER: Cambridge University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This paper investigated whether the highly selective norepinephrine reuptake inhibitor reboxetine leads to a dose-dependent cortisol release and whether this response depends on

personality dimensions related to clin. depression in healthy volunteers. Male subjects received placebo or 2 or 4 mg reboxetine in a balanced, randomized cross-over study. Cortisol was measured in saliva. Furthermore, several measurements of cardiovascular parameters, emotional states, and possible side effects were obtained. The subjects were divided into two groups scoring above or below the median of a depressiveness questionnaire scale (low (D-) or high (D+)). Reboxetine stimulated cortisol release. Blood pressure was not affected, but heart rate increased after both doses but not dose dependently. The subjects reported nonspecific arousal, while tiredness-wakefulness and pos.-neg. emotional states were not affected by the drug. Somatic complaints were few, and only nonspecific complaints were elevated but to a negligible extent.. Subjects classified as D+ can be characterized as high responders to the drug. This is especially true not only with respect to cortisol increases but also to changes in heart rate and some ratings of phys. complaints. Hot flushes, sweating and a throbbing sensation in blood vessels in the head were observed in D+ subjects but only with the 4-mg dose. The results demonstrate that reboxetine stimulates cortisol release and heart rate and that this is particularly pronounced in subjects scoring high on depression-related personality dimensions. Reboxetine, therefore, is a promising tool for investigating neuroendocrine response to noradrenergic challenge tests. The question whether the increased responses in D+ subjects are due to an up-regulation of receptor sensitivity as a consequence of low norepinephrine supply is discussed.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L2 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:175494 CAPLUS Full-text

DOCUMENT NUMBER: 130:347560

TITLE: The effect of ovariectomy and estrogen replacement on

AUTHOR(S): small artery biomechanics in the rat
Acs, Nandor; Szekacs, Bela; Nadasy, Gyorgy L.;
Varbiro, Szabolcs; Kakucs, Reka; Monos, Emil
CORPORATE SOURCE: 2nd Department of Obstetrics and Gynaecology,
Semmelweis University of Medicine, Budapest,

Hung.

SOURCE: British Journal of Obstetrics and Gynaecology
(

1999), 106(2), 148-154

CODEN: BJOGAS; ISSN: 0306-5456

Blackwell Science Ltd.

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

Journal

English

AB Objective To determine the effects of estrogen deficiency and hormone replacement therapy on the biomech. properties of a small artery. Sample Thirty non-pregnant female Sprague-Dawley rats. Methods Twenty animals were pharmacol. ovariectomized by triptorelin and received either estradiol propionate or its vehicle. Ten other animals received only the vehicle for the same period of time (control group). After 12 wk of treatment,

cylindrical segments of the saphenous artery were isolated and cannulated at both ends. Pressure-diameter curves were recorded from segments in normal Krebs-Ringer, using norepinephrine, and then with papaverine. The vessel segment close to the examined one was histol. evaluated. Serum levels of estradiol and cortisol were determined. Main outcome measures Biomech. parameters based on the pressure-diameter curves. Results Pharmacol. ovariectomy decreased the passive diameter of the arteries and estrogen replacement therapy prevented this. Decreased reactivity to norepinephrine was also restored by estrogen treatment. Pressure induced myogenic tone was decreased significantly by oophorectomy and increased after estradiol treatment. No significant changes were found in wall thickness, distensibility, elastic modulus or tangential stress. No significant histol. alterations were seen in the vessel wall. Estradiol levels were significantly decreased in the castrated animals compared with the other two groups. Conclusions These results suggest that estrogen deficiency decreases and estrogen replacement increases the passive diameter of small peripheral arteries, and that estrogen enhances the reactivity of vascular smooth muscle. These responses may provide the background mechanisms for the increased incidence of arterial hypertension and hot flashes during the menopause and the ability of estrogen substitution to prevent them.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L2 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1991:422291 CAPLUS Full-text

DOCUMENT NUMBER: 115:22291

ORIGINAL REFERENCE NO.: 115:3785a,3788a

TITLE: Vasomotor flushes

AUTHOR(S): Walsh, Brian

CORPORATE SOURCE: Dep. Gynecol., Harvard Med. Sch., Boston, MA, 02115,

USA

SOURCE: Annals of the New York Academy of Sciences (1990), 592(Multidiscip. Perspect. Menopause), 346-56

CODEN: ANYAA9; ISSN: 0077-8923

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 41 refs. Hot flashes are a frequent symptom of the menopause and appear to be a consequence of estrogen withdrawal. It has been hypothesized that estrogens act upon the hypothalamic thermoregulatory center, an effect that may be mediated by central neurotransmitters, such as norepinephrine. The effects of various hormone or nonhormone replacements are described.

L2 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1989:206502 CAPLUS Full-text

DOCUMENT NUMBER: 110:206502

ORIGINAL REFERENCE NO.: 110:34135a,34138a

TITLE: Biophysical and endocrine-metabolic changes during

menopausal hot flashes: increase
in plasma free fatty acid and norepinephrine
levels

AUTHOR(S): Cignarelli, M.; Cicinelli, E.; Corso, M.;
Cospite, M. R.; Garruti, G.; Tafaro, E.; Giorgino, R.;
Schonauer, S.

CORPORATE SOURCE: State Univ. Bari, Bari, I-70124, Italy

SOURCE: Gynecologic and Obstetric Investigation (1989
, 27(1), 34-7
CODEN: GOBIDS; ISSN: 0378-7346

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Thermocutaneous, vascular, metabolic and hormonal changes were
investigated during hot flashes in postmenopausal women. The 1st
detectable change was an increase in finger blood flow with a
concomitant enhancement of skin conductance. The increase in skin
conductance was followed rapidly by a sharp rise in finger
temperature. The main endocrine-metabolic changes associated with
the above phenomena were a sharp increase in plasma free fatty
acids (.apprx.65%), norepinephrine (.apprx.100%), and LH
(.apprx.20%) levels. Plasma glucose and cortisol tended to be
increased, but this effect was not significant. Plasma levels of
insulin, glucagon, growth hormone, epinephrine, and dopamine
remained unchanged.

L2 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1985:56459 CAPLUS Full-text

DOCUMENT NUMBER: 102:56459

ORIGINAL REFERENCE NO.: 102:8753a, 8756a

TITLE: Pituitary hormones during the menopausal hot
flash

AUTHOR(S): Meldrum, David R.; Defazio, John D.; Erlik,
Yohanan; Lu, John K. H.; Wolfson, Ada F.; Carlson,
Harold E.; Hershman, Jerome M.; Judd, Howard L.

CORPORATE SOURCE: Dep. Obstetr. Gynecol., Univ. California, Los
Angeles, CA, USA

SOURCE: Obstetrics & Gynecology (New York, NY, United
States) (1984), 64(6), 752-6
CODEN: OBGNAS; ISSN: 0029-7844

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Postmenopausal women with severe hot flashes had continuous
recordings of finger temperature and skin resistance as objective
indexes of flushing episodes, and serial measurements of anterior
pituitary hormones as indirect indexes of hypothalamic neurotransmitter
activity. Increases of growth hormone [9002-72-6], ACTH [9002-60-2],
and LH [9002-67-9] occurred with maximal concns. at 30, 5, and 15 min,
resp., after the onset of the skin temperature rises. No fluctuations
of prolactin, TSH, or FSH were observed. The mean serum cortisol [50-
23-7] concentration increased 15 min after the hot flash, presumably

consequent to the preceding elevation of ACTH. Pituitary ACTH release may be secondary to hypothalamic cooling, whereas increased growth hormone and LH output and the thermoregulatory adjustments comprising the flushing episodes are all consistent with cyclic episodes of increased hypothalamic norepinephrine activity.

=> s 15 and ('hot flush?' or 'hot flash?' or 'sweat?' or dilat?)

1458 L5
492593 'HOT'
52 'HOTS'
492641 'HOT'
('HOT' OR 'HOTS')
7436 'FLUSH'
1240 'FLUSHES'
8442 'FLUSH'
('FLUSH' OR 'FLUSHES')
553 'HOT FLUSH?'
('HOT' (W) 'FLUSH')
492593 'HOT'
52 'HOTS'
492641 'HOT'
('HOT' OR 'HOTS')
65236 'FLASH'
4690 'FLASHES'
67784 'FLASH'
('FLASH' OR 'FLASHES')
1072 'HOT FLASH?'
('HOT' (W) 'FLASH')
7802 'SWEAT'
200 'SWEATS'
7966 'SWEAT?'
('SWEAT' OR 'SWEATS')
63270 DILAT?

L6 10 L5 AND ('HOT FLUSH?' OR 'HOT FLASH?' OR 'SWEAT?' OR DILAT?)

=> d 16 ibib abs 1-10

L6 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:734249 CAPLUS Full-text
DOCUMENT NUMBER: 149:79614

TITLE: Aryl sulfamide derivatives as monoamine reuptake

inhibitors and their preparation and methods

use
INVENTOR(S): McComas, Casey Cameron; Cohn, Stephen Todd;
Crawley, Matthew L.; Fensome, Andrew; Goldberg, Joel
Adam; Jenkins, Douglas John; Kim, Callain Younghee;
Mahaney, Paige Erin; Mann, Charles William; Marella,
Michael Anthony; O'Neill, David John; Sabatucci,
Joseph P.; Terefenko, Eugene Anthony; Trybulski, Eugene

John; Vu,

An Thien; Woodworth, Richard Page, Jr.; Zhang,

Puwen

PATENT ASSIGNEE(S):

Wyeth, John, and Brother Ltd., USA

SOURCE:

PCT Int. Appl., 437pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

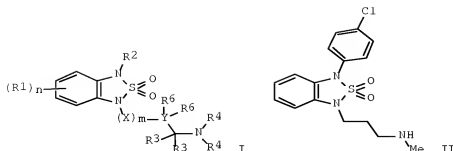
FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2008073459	A1	20080619	WO 2007-US25405	
20071212				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY,				
BZ, CA,				
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ES, FI,				
GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,				
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KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,				
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TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,				
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IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK,				
TR, BF,				
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,				
TG, BW,				
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,				
AM, AZ,				
BY, KG, KZ, MD, RU, TJ, TM				
US 20080161366	A1	20080703	US 2007-955195	
20071212				
US 20080167303	A1	20080710	US 2007-955018	
20071212				
US 20080194654	A1	20080814	US 2007-955204	
20071212				
PRIORITY APPLN. INFO.:			US 2006-869644P	P
20061212				
OTHER SOURCE(S):		MARPAT 149:79614		
GI				



AB The invention is directed to aryl sulfamide derivs. of formula I: or a pharmaceutically acceptable salt, stereoisomer or tautomer thereof, which are monoamine reuptake inhibitors, compns. containing these derivs., and methods of their use for the prevention and treatment of conditions, including, inter alia, vasomotor symptoms, sexual dysfunction, gastrointestinal disorders and genitourinary disorder, depression disorders, endogenous behavioral disorders, cognitive disorders, diabetic neuropathy, pain, and other diseases or disorders. Compds. of formula I wherein n is 0 to 4; m is 0 to 6; each X is independently (un)substituted methylene, NH and derivs., O, S, SO, and SO₂; Y is C; Y and adjacent X taken together to form (un)substituted ethenylene, C.tplbond.C, and (un)substituted aryene; each R₁ is independently H, C₁-6 alkyl, C₁-6 alkoxy, halo, CF₃, OCF₃, OH, C₁-5 alkanoyloxy, NO₂, CN, C₂-6 alkenyl, etc.; R₂ is (un)substituted C₆-10 aryl and (un)substituted heteroaryl; each R₃ is independently H, halo, OH, (un)substituted C₁-6 alkyl, heterocyclic ring, (un)substituted C₆-10 aryl, and (un)substituted heteroaryl; R₃R₃ taken together to form =O; each R₄ is independently H, (un)substituted C₁-6 alkyl, (un)substituted C₇-16 aralkyl, and (un)substituted heteroarylmethyl; each R₆ is independently H, C₁-4 alkyl, C₁-6 alkoxy, halo, OH, (un)substituted C₆-10 aryl, and (un)substituted heteroaryl; R₆R₆ taken together to form a cycloalkyl, heterocyclic ring, =O, and =N-OH; and their pharmaceutically acceptable salts, stereoisomers and tautomers thereof, are claimed. Example compound II•HCl was prepared by cyclization of N-(4-chlorophenyl)benzene-1,2-diamine with sulfamide; the resulting 1-(4-chlorophenyl)-1,3-dihydro-2,1,3-benzothiadiazole 2,2-dioxide coupling alkylation with 3-bromopropanol to give 1-(3-bromopropyl)-3-(4-chlorophenyl)-1,3-dihydro-2,1,3-benzothiadiazole 2,2-dioxide, which underwent amination with ammonia to give II, which was converted to its hydrochloride salt. All the invention compds. were evaluated for their monoamine reuptake inhibitory activity (data given).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2008:95116 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 148:160156

TITLE: Biomarker-optimized attention deficit-hyperactivity

disorder (ADHD) treatment with selective norepinephrine reuptake inhibitors
Lawrence, Donald Gilbert

INVENTOR(S):
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080020387	A1	20080124	US 2007-694099	
20070330				
PRIORITY APPLN. INFO.:			US 2006-788008P	P
20060331				

AB The invention provides methods for predicting patient responsiveness to treatment of attention-deficit/hyperactivity disorder (ADHD) with selective norepinephrine reuptake inhibitors; identifying individuals requiring a higher than normal dose of atomoxetine for treating ADHD; and predicting patient responsiveness to treatment of neuropsychiatric diseases or disorders responsive to treatment with selective norepinephrine reuptake inhibitors are provided. These methods are based on the identification of the variable number of tandem repeats (VNTR) polymorphism present in the 3'-untranslated region of the human dopamine transporter 1 (DAT 1) gene present in patient body fluid or tissue samples. Patients with a 10/10 VNTR genotype are considered poor responders to treatment with atomoxetine and other selective norepinephrine reuptake inhibitors for the indicated conditions.

L6 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:94908 CAPLUS Full-text

DOCUMENT NUMBER: 148:191944

TITLE: Preparation of N-spiroimidazolidineindenyl heteroaryl

amides as CGRP receptor antagonists
INVENTOR(S): Gutierrez, Corey Don; Termin, Andreas; Joshi, Pramod;

Sanghee; Hadida Ruah, Sara; Bergeron, Daniele; Yoo,

Cao, Jingrong

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 74pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2008011190
20070723

A1

20080124

WO 2007-US16559

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY,
BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,
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KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,
MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

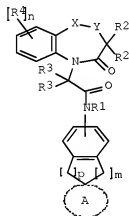
US 2006-832397P P

20060721

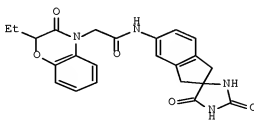
OTHER SOURCE(S):

MARPAT 148:191944

GI



I



II

AB The title compds. I [X = O, NR1, S, SO, SO2; R1 = H, alkyl; ring A = (un)substituted 4-7 membered heterocyclic ring having 1-4 heteroatoms selected from O, N, S, SO or SO2 (optionally fused to other ring); m, p = 1-3; n = 1-4; Y = a bond, C(R2)2 or C(R2)2C(R2)2; R2 = H, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, etc.], useful as CGRP receptor antagonists, were

prepared E.g., a multi-step synthesis of II, starting from 2-indanone, was given. Exemplified compds. I were found to be antagonists of CGRP in the I125-CGRP binding assay and in the CGRP functional antagonism assay (no specific data given). The present invention relates also to pharmaceutical compns. comprising compds. I and to methods for treating CGRP receptor-mediated diseases and conditions.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L6 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2007:1447778 CAPLUS Full-text
 DOCUMENT NUMBER: 148:79043
 TITLE: 2-Anilino-4-(heterocyclic) amino-pyrimidines compounds

as PKC- α inhibitors and their preparation, pharmaceutical compositions and use in the

treatment

of cardiovascular and other diseases
 Djung, Jane Far-Jine; Golebiowski, Adam;

INVENTOR(S):
 Hunter, Jack

A.; Shrum, Gary P.

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 45pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

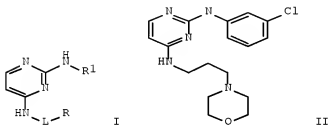
English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070293494	A1	20071220	US 2007-762394	
20070613				
WO 2007146981	A2	20071221	WO 2007-US71077	
20070613				
WO 2007146981	A3	20080221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
HU, IE, RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,				

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
 TG, BW,
 GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
 AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
 PRIORITY APPLN. INFO.: US 2006-813956P P
 20060615
 OTHER SOURCE(S): MARPAT 148:79043
 GI



AB The invention relates to 2-arylamino-4-(heterocyclic)aminopyrimidines of formula I which are inhibitors and therefore inhibit Protein Kinase C- α (PKC- α). The PKC- α inhibitors of the present invention are important for improving myocardial intracellular calcium cycling, resulting in improved myocardial contraction and relaxation performance and thereby slowing the progression of heart failure. The present invention further relates to compns. comprising said 2-arylamino-4-(heterocyclic)amino-pyrimidines and to methods for controlling, abating, or otherwise slowing the progression of heart failure. Compds. of formula I wherein R is (un)substituted 3- to 7-membered heterocyclic unit; L is a linking group; R1 is (un)substituted phenyl; are claimed. Example compound II was prepared by methylation of thiouridine with Me iodide; the resulting 2-(methylthio)pyrimidin-4(3H)-one underwent amination with 3-chloroaniline to give 2-(3-chlorophenylamino)pyrimidin-4(3H)-one, which underwent chlorination to give 4-chloro-N-(3-chlorophenyl)pyrimidin-2-amine, which underwent substitution with 3-morpholinopropylamine to give compound II. All the invention compds. were evaluated for their PKC- α inhibitory activity. From the assay, it was determined that compound II exhibited an IC50 value of 2 nM.

L6 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2007:815018 CAPLUS Full-text
 DOCUMENT NUMBER: 147:211728
 TITLE: Preparation of sulfonyl substituted 1H-indoles
 as
 ligands for the 5-hydroxytryptamine receptors,
 particularly 5-HT6 and 5-HT2A receptors, and
 inhibitors of norepinephrine reuptake
 INVENTOR(S): McDewitt, Robert E.; Li, Yanfang; Robichaud,

Albert

PATENT ASSIGNEE(S): J.; Heffernan, Gavin D.; Coghlan, Richard D.; Bernotas, Ronald C.
SOURCE: Wyeth, John, and Brother Ltd., USA
PCT Int. Appl., 129pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007084841	A2	20070726	WO 2007-US60454	
20070112				
WO 2007084841	A3	20070913		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2007206016	A1	20070726	AU 2007-206016	
20070112				
CA 2636007	A1	20070726	CA 2007-2636007	
20070112				
US 20070203120	A1	20070830	US 2007-622649	
20070112				
EP 1973876	A2	20081001	EP 2007-710091	
20070112				
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
IN 2008DN05932	A	20081024	IN 2008-DN5932	
20080708				
NO 2008003057	A	20081003	NO 2008-3057	
20080709				
KR 2008114688	A	20081231	KR 2008-719566	
20080808				
PRIORITY APPLN. INFO.:			US 2006-758833P	P

20060113

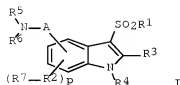
WO 2007-US60454 W

20070112

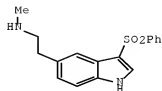
OTHER SOURCE(S):

MARPAT 147:211728

GI



I



II

AB Title compds. I [A = (un)substituted alkylene, alkenylene or alkynylene; R1 = (un)substituted alkyl, (hetero)cycloalkyl, (hetero)aryl, etc.; each R2 independently = bond, O, S, CO, C(O)O, etc.; R3 and R4 independently = H, (un)substituted alkyl, (hetero)cycloalkyl, (hetero)aryl, etc.; R5 and R6 independently = H, (un)substituted alkyl, haloalkyl, alkenyl, etc.; R5 and R6 may join together with N to form a 3- to 8-membered heterocycloalkyl ring or a 5- to 8-membered heteroaryl ring; each R7 independently = H, halo, CN, NO2, etc., p = 0-3], and their pharmaceutically acceptable salts, are prepared and disclosed as ligands for the 5-hydroxytryptamine (5-HT) receptors, especially 5-HT6 and 5-HT2A receptors, and as inhibitors of norepinephrine reuptake. Thus, e.g., II was prepared in multi-step synthesis via cyclization of Me [2-[4-amino-3-[(phenylsulfonyl)methyl]phenyl]ethyl]methylcarbamate (preparation given) followed by deprotection. I showed a high degree of affinity for the 5-HT6 receptor, e.g., II demonstrated Ki value of 5.2 nM for 5-HT6 binding affinity. As modulators of the 5-HT6 and 5-HT2A receptors and inhibitors of norepinephrine reuptake, I are useful in the treatment of disorders related to or associated with the 5-HT receptors or with norepinephrine reuptake inhibition.

L6 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:510613 CAPLUS Full-text

DOCUMENT NUMBER: 145:8035

TITLE: 4-Piperidinecarboxamides as modulators of vanilloid

pharmaceutical and

receptor VR1, their preparation,

INVENTOR(S):

veterinary compositions, and use in therapy
Calvo, Raul R.; Wing, Cheung S.; Player, Mark R.

PATENT ASSIGNEE(S):

Janssen Pharmaceutica N.V., Belg.

SOURCE:

PCT Int. Appl., 197 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006058338	A2	20060601	WO 2005-US43192	
20051129				
WO 2006058338	A3	20070405		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LI, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20060116368	A1	20060601	US 2005-288624	
20051129				
PRIORITY APPLN. INFO.:			US 2004-631436P	P
20041129				
20050830			US 2005-712496P	P
20051101			US 2005-732035P	P
OTHER SOURCE(S):		CASREACT 145:8035; MARPAT 145:8035		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to 4-piperidinecarboxamides I, which are vanilloid receptor 1 (VR1) modulators. In compds. I, Ar is selected from benzo[b]thienyl, naphthyl, biphenyl, isoquinolinyl, thienyl, pyridazinyl, and benzothiazolyl; Z is O or S; n is 1 or 2; each R1 is independently selected from H, C1-6 alkyl, -CO2R3, and -CH2CO2R3, where R3 is H or C1-3 alkyl; and R2 is H or C1-6 alkyl, optionally substituted with -OR3; including stereoisomers, tautomers, solvates and salts thereof. The invention also relates to the preparation of I, pharmaceutical or veterinary compns. comprising a compound I admixed with a

pharmaceutically/veterinarily acceptable carrier, excipient, or diluent, as well as to the use of the compns. for the treatment or prevention of conditions responding to the modulation of VR1. Substitution of 3-bromo-1,2-dimethylbenzene with Et nipecotate and ester hydrolysis gave carboxylic acid II, which was amidated with 6-amino-2H-1,4-benzoxazin-3(4H)-one to give piperidinecarboxamide III. The compds. of the invention are modulators of VR1, e.g., compound III expresses a K_i value of 27 nM for binding to VR1 and an IC50 value of 0.06 μ M for inhibition of VR1 function.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L6 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:588645 CAPLUS Full-text

DOCUMENT NUMBER: 143:115550

TITLE: Preparation of heterocyclic compounds as selective

treating norepinephrine reuptake inhibitors for

general hot flashes, impulse control disorders and personality change due to a

medical condition

INVENTOR(S): Allen, Albert John; Hemrick-Luecke, Susan; Sumner,

Calvin Russell; Wallace, Owen Brendan

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 337 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005060949	A2	20050707	WO 2004-US38221	
20041201				
WO 2005060949	A3	20050909		
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CA, CH,				
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GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
NA, NI,				
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				
SL, SY,				
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,				
ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,				
ZW, AM,				
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DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2548304 A1 20050707 CA 2004-2548304

20041201 EP 1729754 A2 20061213 EP 2004-811076

20041201 EP 1729754 B1 20080702

HU, IE, R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

CN 1889940 A 20070103 CN 2004-80036841

20041201 JP 2007513945 T 20070531 JP 2006-543830

20041201 AT 399557 T 20080715 AT 2004-811076

20041201 ES 2307071 T3 20081116 ES 2004-811076

20041201 US 20070015786 A1 20070118 US 2006-581015

20060530 KR 2006121178 A 20061128 KR 2006-711571

20060612

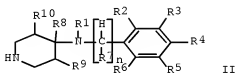
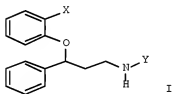
PRIORITY APPLN. INFO.: US 2003-529428P P

20031212 WO 2004-US38221 W

20041201

OTHER SOURCE(S): CASREACT 143:115550; MARPAT 143:115550

GI



AB The invention relates to a method of preventing or treating hot flashes, vasomotor symptoms, impulse control disorders or personality change due to a general medical condition, comprising administering to a patient in need thereof a therapeutically effective amount of a selective norepinephrine reuptake inhibitor selected from atomoxetine, reboxetine, I [X = alkylthio; Y = alkyl], II [n = 1-3; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2-R4 = H, alkyl, alkoxy, etc.; R5-R6 = H, alkyl, alkoxy, halo; R7-R8 = H, alkyl; R9-R10 = H, halo, OH, CN, alkyl, alkoxy], etc. Over 200 title compds. such as I, II and other heterocyclic compds. disclosed, were prepared E.g., a 2-step synthesis of N-(2-methylpropyl)-N-[(2-fluorophenyl)methyl]piperidin-4-amine

fumarate, starting from tert-Bu 4-(2-methylpropylamino)piperidine-1-carboxylate and 2-fluorobenzaldehyde, was given. The preferred exemplified title compds. exhibit a Ki value less than 1 μ M, more preferably less than 500 nM at the norepinephrine transporter as determined using the scintillation proximity assay.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

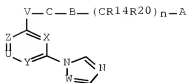
RE FORMAT

L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2002:610405 CAPLUS Full-text
 DOCUMENT NUMBER: 137:169534
 TITLE: Preparation of imidazolyl pyrimidinamines as
 NOS inhibitors
 INVENTOR(S): Arnaiz, Damian O.; Baldwin, John J.; Davey,
 David D.;
 Devlin, James J.; Dolle, Roland Ellwood, III;
 Erickson, Shawn David; McMillan, Kirk;
 Morrissey, Michael M.; Ohlmeyer, Michael H. J.; Pan,
 Gonghua; Paradkar, Vidyadhar Madhav; Parkinson, John;
 Phillips, Gary B.; Ye, Bin; Zhao, Zuchun
 PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA; Pharmacoepia,
 Inc.
 SOURCE: U.S., 132 pp., Cont.-in-part of U.S. Ser. No.
 25,124,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6432947	B1	20020813	US 1999-383813	
19990826				
CN 1100777	C	20030205	CN 1998-804281	
19980219				
AT 345339	T	20061215	AT 1998-906555	
19980219				
EP 1754703	A2	20070221	EP 2006-23449	
19980219				
EP 1754703	A3	20070228		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU,				
MC, NL,				
PT, SE				
ES 2277382	T3	20070701	ES 1998-906555	
19980219				
CA 2376355	A1	20010301	CA 2000-2376355	
20000824				
WO 2001014371	A1	20010301	WO 2000-US23173	

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 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
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 GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
 RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
 UZ, VN,
 YU, ZA, ZW
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 CH, CY,
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 BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 BR 2000014144 A 20020521 BR 2000-14144
 20000824
 EP 1206467 A1 20020522 EP 2000-959333
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 EP 1206467 B1 20031217
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 SI 20818 A 20020831 SI 2000-20040
 20000824
 HU 2002002450 A2 20021128 HU 2002-2450
 20000824
 HU 2002002450 A3 20031229
 EE 200200091 A 20030415 EE 2002-91
 20000824
 NZ 517411 A 20030926 NZ 2000-517411
 20000824
 AT 256681 T 20040115 AT 2000-959333
 20000824
 AU 769405 B2 20040129 AU 2000-70671
 20000824
 PT 1206467 T 20040531 PT 2000-959333
 20000824
 ES 2213599 T3 20040901 ES 2000-959333
 20000824
 CN 1206228 C 20050615 CN 2000-814669
 20000824
 RU 2277094 C2 20060527 RU 2002-107203
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 ZA 2002001485 A 20030521 ZA 2002-1485
 20020221
 IN 2002MN00232 A 20050318 IN 2002-MN232
 20020225
 NO 2002000925 A 20020416 NO 2002-925
 20020226
 NO 323886 B1 20070716
 MX 2002002022 A 20021031 MX 2002-2022
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 BG 106440 A 20021129 BG 2002-106440
 20020226

HR 2002000175	B1	20080731	HR 2002-175	
20020227				
LT 4982	B	20030127	LT 2002-28	
20020315				
LV 12887	B	20030120	LV 2002-50	
20020326				
US 20020165203	A1	20021107	US 2002-121886	
20020412				
US 6841673	B2	20050111		
US 20020183323	A1	20021205	US 2002-121659	
20020412				
US 6864263	B2	20050308		
US 20030004137	A1	20030102	US 2002-121379	
20020412				
US 6747031	B2	20040608		
US 20030027794	A1	20030206	US 2002-121758	
20020412				
US 6846829	B2	20050125		
US 20030060452	A1	20030327	US 2002-121212	
20020412				
US 6849739	B2	20050201		
US 20030069210	A1	20030410	US 2002-122072	
20020412				
US 6841674	B2	20050111		
US 20030073669	A1	20030417	US 2002-121682	
20020412				
US 20030078265	A1	20030424	US 2002-121808	
20020412				
US 6670473	B2	20031230		
US 20030083332	A1	20030501	US 2002-122047	
20020412				
US 6887865	B2	20050503		
US 20030092678	A1	20030515	US 2002-122006	
20020412				
US 6864368	B2	20050308		
HK 1051683	A1	20060127	HK 2003-103750	
20030527				
PRIORITY APPLN. INFO.:			US 1997-808975	B2
19970219				
			US 1998-25124	B2
19980217				
			EP 1998-906555	A3
19980219				
			WO 1998-US3176	A
19980219				
			US 1999-383813	A
19990826				
			WO 2000-US23173	W
20000824				
OTHER SOURCE(S):	MARPAT 137:169534			
GI				



I

AB The title compds. [I; U = N, CR5 (R5 = H, halo, alkyl, optionally substituted aralkyl or aryl, etc.); V = NR4, S, O, CHR4 (R4 = H, alkyl, aryl, aralkyl, cycloalkyl); W = N, CH; X, Y, Z = N, CR19 (R19 = H, alkyl, cyclopropyl, halo, haloalkyl); A = R1, OR1, CONR1R2, PO(NR1R2)2, NR1COR2, etc. (R1, R2 = H, optionally substituted alkyl or cycloalkyl, etc. or NR1R2 = N-heterocyclyl); B = CR17(CHR15)mQR3 (m = 1-4, R3 = H, alkyl, cycloalkyl, optionally substituted aryl, etc.; R15, R17 = H, alkyl; Q = CO, O, C:NR1, etc.); C = (CHR12)q(CHR13)r (q, r = 0-1; R12, R13 = H, alkyl); or B = C = null; R14, R20 = H, alkyl; n = 1-3], useful as inhibitors of nitric oxide synthase, were prepared. Thus, N-[(1,3-benzodioxol-5-yl)methyl]-1-[3-(1H-imidazol-1-yl)phenyl]piperidine-2-acetamide was prepared by reaction of 1-(3-aminophenyl)imidazole, Et 7-chloro-3-oxoheptanoate, and piperonylamine. All exemplified compds. I showed iNOS inhibitory activity at concns. less than 25 μ M.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L6 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:604917 CAPLUS Full-text

DOCUMENT NUMBER: 129:231019

ORIGINAL REFERENCE NO.: 129:47015a, 47018a

TITLE: Preparation of N-heterocyclic derivatives as NOS

inhibitors

INVENTOR(S): Arnaiz, Damian O.; Baldwin, John J.; Davey, David D.;

Devlin, James J.; Dolle, Roland Ellwood, III; Erickson, Shawn David; McMillan, Kirk;

Morrissey,

Michael M.; Ohlmeyer, Michael H. J.; Pan,

Gonghua;

Paradkar, Vidyadhar Madhav; Parkinson, John;

Phillips,

Gary B.; Ye, Bin; Zhao, Zuchun; et al.

PATENT ASSIGNEE(S): Berlex Laboratories, Inc., USA; Pharmacopeia, Inc.; et

al.

SOURCE: PCT Int. Appl., 358 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

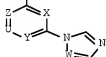
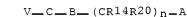
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9837079	A1	19980827	WO 1998-US3176	
19980219				
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LI, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2281545	A1	19980827	CA 1998-2281545	
19980219				
CA 2281545	C	20070424		
AU 9861749	A	19980909	AU 1998-61749	
19980219				
AU 732969	B2	20010503		
EP 968206	A1	20000105	EP 1998-906555	
19980219				
EP 968206	B1	20061115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
GB 2338957	A	20000112	GB 1999-19686	
19980219				
NZ 337861	A	20010223	NZ 1998-337861	
19980219				
HU 2002004228	A2	20030328	HU 2002-4228	
19980219				
HU 2002004228	A3	20030528		
RU 2241708	C2	20041210	RU 1999-120077	
19980219				
EP 1754703	A2	20070221	EP 2006-23449	
19980219				
EP 1754703	A3	20070228		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
NO 9903996	A	19991018	NO 1999-3996	
19990819				
NO 321664	B1	20060619		
MX 9907670	A	20011213	MX 1999-7670	
19990819				
HK 1025952	A1	20020412	HK 2000-104236	
20000711				
US 20030027794	A1	20030206	US 2002-121758	
20020412				

US 6846829	B2	20050125		
US 20030060452	A1	20030327	US 2002-121212	
20020412				
US 6849739	B2	20050201		
US 20030069210	A1	20030410	US 2002-122072	
20020412				
US 6841674	B2	20050111		
PRIORITY APPLN. INFO.:			US 1997-808975	A2
19970219				
			US 1998-25124	A
19980217				
			EP 1998-906555	A3
19980219				
			WO 1998-US3176	W
19980219				
			US 1999-383813	A3
19990826				
OTHER SOURCE(S):	MARPAT	129:231019		
GI				



I

AB N-Heterocyclic derivs. I [U = N, CR5 (R5 = H, halo, alkyl, optionally substituted aralkyl or aryl, etc.); V = NR4, S, O, CHR4 (R4 = H, alkyl, aryl, aralkyl, cycloalkyl); W = N, CH; X, Y, Z = N, CR19 (R19 = H, alkyl, cyclopropyl, halo, haloalkyl); A = R1, OR1, CONR1R2, PO(NR1R2)2, NR1COR2, etc. (R1, R2 = H, optionally substituted alkyl or cycloalkyl, etc. or R1R2N = N-heterocyclyl); B = CR17(CHR15)mQR3 (m = 1-4, R3 = H, alkyl, cycloalkyl, optionally substituted aryl, etc.; R15, R17 = H, alkyl; Q = CO, O, C:NR1, etc.); N-heterocyclyl; C = (CHR12)q(CHR13)r (q, r = 0 or 1; R12, R13 = H, alkyl); or B = C = null; R14, R20 = H, alkyl; n = 1-3] were prepared as inhibitors of nitric oxide synthase. Thus, N-[(1,3-benzodioxol-5-yl)methyl]-1-[3-(1H-imidazol-1-yl)phenyl]piperidine-2-acetamide was prepared by reaction of 1-(3-aminophenyl)imidazole, 7-chloro-3-oxoheptanoic acid Et ester, and piperonylamine.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L6 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2009 ACS on SIN
 ACCESSION NUMBER: 1974:146178 CAPLUS Full-text
 DOCUMENT NUMBER: 80:146178
 ORIGINAL REFERENCE NO.: 80:23593a,23596a
 TITLE: 1,4-Benzenedisulfonamide

INVENTOR(S): Cross, Peter E.; Gadsby, Brian
 PATENT ASSIGNEE(S): Pfizer Corp.
 SOURCE: Ger. Offen., 14 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2340010	A1	19740314	DE 1973-2340010	
19730807				
GB 1380009	A	19750108	GB 1972-37720	
19720812				
AT 7306915	A	19751115	AT 1973-6915	
19730807				
AT 331248	B	19760810		
BE 803373	A1	19740208	BE 1973-134373	
19730808				
NL 7311000	A	19740214	NL 1973-11000	
19730809				
NL 162641	B	19800115		
NL 162641	C	19800616		
AU 7359084	A	19750213	AU 1973-59084	
19730809				
US 3867390	A	19750218	US 1973-386854	
19730809				
FR 2195449	A1	19740308	FR 1973-29377	
19730810				
ZA 7305474	A	19740828	ZA 1973-5474	
19730810				
CA 978945	A1	19751202	CA 1973-178508	
19730810				
SE 385008	B	19760531	SE 1973-10996	
19730810				
JP 49085066	A	19740815	JP 1973-90450	
19730811				
JP 59000508	B	19840107		
IN 139006	A1	19760424	IN 1973-CA1864	
19730813				
US 3932639	A	19760113	US 1974-512007	
19741004				
US 3932636	A	19760113	US 1974-512010	
19741004				
US 3932649	A	19760113	US 1974-512012	
19741004				
US 3957796	A	19760518	US 1974-512009	
19741004				
US 3974155	A	19760810	US 1974-512008	
19741004				
JP 57131774	A	19820814	JP 1981-116291	
19810724				
JP 58057431	B	19831220		
PRIORITY APPLN. INFO.:			GB 1972-37720	A
19720812				

19720812	GB 1972-33720	A
19720812	GB 1973-37720	A
19730809	US 1973-386854	A3
19730811	JP 1973-90450	A

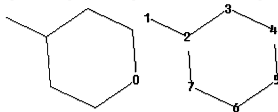
GI For diagram(s), see printed CA Issue.

AB Twenty-three disulfonamides I (X = CH₂, CHOH, CH₂CH₂, O, or CH₂O; Rn1 = H, 3- or 4-MeO, 2,6-Me₂, 4,4-ethylenedioxy, 2-Me, 2-Et, 2,6-Et₂, 2,6-ethylene, or 2,3-tetramethylene; R2 = 2- or 3-Cl, 2-F, 2-Br, or 2-F3C), useful as cerebral vasodilators, were prepared by reaction of the sulfonyl chlorides II with excess RH.

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10581015_224_2.str



chain nodes :

1

ring nodes :

2 3 4 5 6 7

chain bonds :

1-2

ring bonds :

2-3 2-7 3-4 4-5 5-6 6-7

exact/norm bonds :

2-3 2-7 3-4 4-5 5-6 6-7

exact bonds :

1-2

Match level :

1:CLASS 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom

L4 STRUCTURE UPLOADED

=> d l4

L4 HAS NO ANSWERS

L4 STR



<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l5 and (norepinephrin? or NRI? or ?epinephrin?)

6995 L5

51075 NOREPINEPHRIN?

1020 NRI?

66802 ?EPINEPHRIN?

L6 30 L5 AND (NOREPINEPHRIN? OR NRI? OR ?EPINEPHRIN?)

=> s l6 and (py<2003 or ay<2003 or pry<2003)

22983475 PY<2003

4504208 AY<2003

3973137 PRY<2003

L7 7 L6 AND (PY<2003 OR AY<2003 OR PRY<2003)

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L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:325699 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:392292

TITLE: Preparation of heterocyclic compounds, e.g., N-alkylpiperidin-3-yl substituted analogs as

ligands

treating

for monoamine receptors and transporters for

drug addiction or drug dependence

INVENTOR(S): Aquila, Brian M.; Bannister, Thomas D.; Cuny, Gregory

D.; Hauske, James R.; Holland, Joanne M.;

Persons,

Paul E.; Radeke, Heike S.; Wang, Fengjiang;

Shao,

Liming

PATENT ASSIGNEE(S): Sepracor, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 161 pp., Cont.-in-part of U.S.

Ser. No. 607,457.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	----
US 20050080078	A1	20050414	US 2004-771519	

20040204 <--
 US 7294637 B2 20071113
 US 20030050309 A1 20030313 US 2001-951130
 20010912 <--
 US 20040077706 A1 20040422 US 2003-607457
 20030626 <--
 US 7132551 B2 20061107
 WO 2005077463 A2 20050825 WO 2005-US3629
 20050204
 WO 2005077463 A3 20060126
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
 CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
 GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
 KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
 NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
 ZM, ZW, SM
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL,
 PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG
 PRIORITY APPLN. INFO.: US 2000-231667P P
 20000911 <-- US 2001-273530P P
 20010305 <-- US 2001-298057P P
 20010613 <-- US 2001-951130 A3
 20010912 <-- US 2003-607457 A2
 20030626 US 2004-771519 A
 20040204
 OTHER SOURCE(S): MARPAT 142:392292
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. (4 Markush structures given), e.g., I [X = C(R3)2,
 O, SO0-2, NR2, NC(O)R7, NC(O)OR2, NS(O)2R7, C=O; Z = C(R3)2, C(O),
 O, NR, NC(O)OR, SO0-2; m = 1-5; n = 1-2; p = 0-2; q = 0-3; R = H,
 (cyclo)alkyl, (hetero)aryl, aralkyl, heteroaralkyl; R1 = H, alkyl,
 (hetero)aryl, aralkyl, heteroaralkyl; R, R1 may be connected

through a covalent bond; R2 = H, alkyl, fluoroalkyl, aryl, heteroaryl, cycloalkyl; R3 = H, alkyl, aryl, OR2, OC(O)R2, CH2OR2, CO2R2; wherein any two instances of R3 may be connected by a covalent tether whose backbone consists of 1, 2, 3, or 4-carbon atoms; R4 = H, alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, OR; R5-6 = H, alkyl, (CH2)qY, aryl, heteroaryl, F, OR2, OC(O)R2, or an instance of CR5R6 taken together is C(O); R7 = (cyclo)alkyl, (hetero)aryl, aralkyl, or heteroaralkyl; R8-9 = H, alkyl, (CH2)qY, (hetero)aryl, F, OR2, OC(O)R2, or an instance of CR8R9 taken together is C(O); Y = OR2, N(R2)2, SOO-2R2, F(O)(OR2)2; any two instances of R2 may be connected through a covalent bond; a covalent bond may connect R4 and an instance of R5 or R6; any two instances of R5 and R6 may be connected through a covalent bond; any two geminal or vicinal instances of R8 and R9 may be connected through a covalent bond; and the stereochem. configuration at any stereocenter of I is R, S or a mixture of these configurations.] were prepared Examples include synthesis of several hundred compds. of structure I, functional assays for norepinephrine (NE), dopamine (DA) and serotonin (5-HT) antagonism, determination of NE, DA and 5-HT reuptake inhibition, spontaneous locomotor activity/antidepressant behavioral assay in rats and the synthesis of a 96-member combinatorial library in which the library compds. were screened for monoamine uptake inhibition. For instance, 3-((4-trifluoromethylphenoxy)methyl)piperidine trifluoroacetate was alkylated with 1-((4-chlorophenyl)cyclobutyl)-2-chloroethanone (preparation given) and the resulting product reduced with NaBH4 to give II. All 4 enantiomers of II were prepared by a stereospecific synthesis, and X-ray crystallog. determination of one enantiomer allowed the absolute stereochem. of III to be assigned. III had EC50 < 10 nM for DA reuptake inhibition compared to nomifensine = 11 nM. I are useful for the treatment of cocaine addiction or methamphetamine addiction.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L7 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:515484 CAPLUS Full-text

DOCUMENT NUMBER: 141:71450

TITLE: Preparation of N,N-disubstituted 4-

aminopiperidines as

inhibitors of monoamine, in particular

serotonin,

norepinephrine, and dopamine reuptake

INVENTOR(S): Clark, Barry Peter; Cases-Thomas, Manuel

Javier;

Gallagher, Peter Thaddeus; Gilmore, Jeremy;

Masters,

John Joseph; Timms, Graham Henry; Whatton,

Maria Ann;

Wood, Virginia Ann

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 204 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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20031125 <---	WO 2004052858	A2	20040624	WO 2003-US35972	
	WO 2004052858	A3	20040812		
CH, CN,	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,				
GD, GE,	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,				
LC, LK,	GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,				
NO, NZ,	LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI,				
TJ, TM,	OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
AM, AZ,	TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
DK, EE,	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,				
SI, SK,	BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,				
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	EP 1569905	A2	20050907	EP 2003-783319	
20031125 <---	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
MC, PT,	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 20060079554	A1	20060413	US 2005-536295	
20050525 <---	PRIORITY APPLN. INFO.:			GB 2002-28482	A
20021206 <---				US 2002-434720P	P
20021218 <---				WO 2003-US35972	W
20031125	OTHER SOURCE(S):	MARPAT 141:71450			
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB Title compds. I [wherein X = (CHR7)n; n = 1-3; R1 =
(un)substituted alkyl, alkenyl, cycloalkyl/alkyl; R2, R3, R4 =
independently (un)substituted CN, halo, alkyl, alkoxy, Ph, OPh;
R2CCR3, R3CCR4 = independently (un)substituted benzene ring; R5,
R6 = independently halo, (un)substituted alkyl, alkoxy; R7, R8 =

independently H, alkyl; R9, R10 = independently halo, OH, CN, alkyl or alkoxy; and their pharmaceutically acceptable salts; with the proviso that N-ethyl-N-benzyl-4-piperidinamine is excluded] were prepared as inhibitors of the serotonin and/or norepinephrine and/or dopamine reuptake. For example, II•fumaric acid was prepared by reductive amination of 2-cyanobenzaldehyde with secondary amine III (preparation given) in 1,2-dichloroethane in the presence of NaBH(OAc)3, BOC-deprotection, and acidulation with fumaric acid. Selected I exhibited Ki < 100 nM for the inhibition of one or more monoamines reuptake. I have a reduced interaction with Cytochrome CYP2D6 as demonstrated in a CYP2D6 substrate and inhibitor assay. I are useful for treating central and/or peripheral nervous system disorders (no data).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:836762 CAPLUS Full-text

DOCUMENT NUMBER: 139:350474

TITLE: Preparation and compositions of nitrosothio (hetero)cyclic nitric oxide donors

INVENTOR(S): Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Lin,

Chia-en; Ranatunga, Ramani R.; Richardson, Stewart K.;

Wang, Tiansheng; Wang, Weiheng; Wey, Shio-wjyi

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

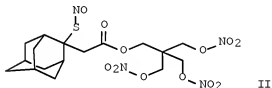
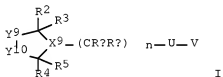
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003086282	A2	20031023	WO 2003-US10562	
20030407 <--				
WO 2003086282	A3	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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 TD, TG
 CA 2480832 A1 20031023 CA 2003-2480832
 20030407 <-- AU 2003223491 A1 20031027 AU 2003-223491
 20030407 <-- US 20030203915 A1 20031030 US 2003-407420
 20030407 <-- EP 1497268 A2 20050119 EP 2003-719621
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 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 JP 2005537223 T 20051208 JP 2003-583309
 20030407 <--
 PRIORITY APPLN. INFO.: US 2002-369873P P
 20020405 <-- WO 2003-US10562 W
 20030407
 OTHER SOURCE(S): MARPAT 139:350474
 GI



AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO2; X9 = CR10 or N; Y9 = CR6R7, NR1, NR25, NR1CR6R7, CR6R7NR1, CR2R3CR6R7, or CR6R7CR2R3; Y10 = CR8R9 or CR8R9CR17R18; R2-R9, R17, and R18 = independently H or alkyl; or R2R3, R4R5, R6R7, or R8R9 = independently oxo; or R4 and R7 together with the C's to which they are attached = cycloalkyl; or CR6R7 = cycloalkyl; R6 and R9 taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R7 and R8 are not present; R4 and R25 taken together with the C and N to which they are attached = heterocyclyl; Ra = lone pair of electrons, H, or (aryl)alkyl; Re and Rf = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CRaRf = heterocyclyl or (bridged) cycloalkyl; Ri = H or (un)substituted alkyl, aryl, carboxamido, sulfonamido, etc.; n = 0-3; and pharmaceutically acceptable salts thereof] were

prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH₂Cl₂ to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC₅₀ of 5 µM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight inhibition, or exhibited much higher IC₅₀ values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:491214 CAPLUS Full-text

DOCUMENT NUMBER: 139:69156

TITLE: Preparation of substituted lactams as tachykinin

antagonists

INVENTOR(S): Middleton, Donald Stuart; Stobie, Alan

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 207 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

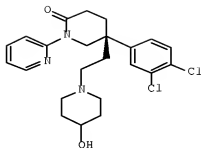
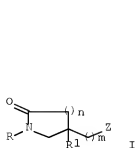
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003051868	A1	20030626	WO 2002-IB5234	

20021206 <--
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
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 GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
 OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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 UG, US, UZ, VN, YU, ZA, ZM, ZW
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 CA 2470236 A1 20030626 CA 2002-2470236
 20021206 <--
 AU 2002366320 A1 20030630 AU 2002-366320
 20021206 <--
 BR 2002015017 A 20040831 BR 2002-15017
 20021206 <--
 EP 1456200 A1 20040915 EP 2002-804985
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 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
 JP 2005514389 T 20050519 JP 2003-552752
 20021206 <--
 US 20040132710 A1 20040708 US 2002-322068
 20021217 <--
 US 7060836 B2 20060613
 MX 2004005221 A 20040819 MX 2004-5221
 20040531 <--
 PRIORITY APPLN. INFO.: GB 2001-30261 A
 20011218 <--
 US 2002-350811P P
 20020122 <--
 WO 2002-IB5234 W
 20021206 <--
 OTHER SOURCE(S): MARPAT 139:69156
 GI



AB Title compds. I [R = 5-7 membered aromatic heterocycle; n = 0-4; m = 1-4; Z = amino] are prepared For instance, (5S)-5-(3,4-Dichlorophenyl)-5-(2,2-dimethoxyethyl)-1-(2-pyridinyl)-2-piperidinone (preparation given) is deprotected (HCl) and condensed with 4-hydroxypiperidine (CH₂Cl₂, NaHB(OAc)₃) to give II. All example compds. have K_i < 1000 nM for the NK₂ receptor. I are useful in treating or preventing a condition for which an NK₂ antagonist is efficacious.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:220550 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:263097

TITLE: Preparation of heterocyclic compounds, e.g., N-alkylpiperidin-3-yl substituted analogs as

ligands

for monoamine receptors and transporters.

INVENTOR(S): Aquila, Brian M.; Bannister, Thomas D.; Cuny, Gregory

D.; Hauske, James R.; Holland, Joanne M.;

Persons,

Paul E.; Radeke, Heike; Wang, Fengjian; Shao,

Liming

PATENT ASSIGNEE(S): Sepracor, Inc., USA

SOURCE: PCT Int. Appl., 275 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022572	A2	20020321	WO 2001-US28654	
20010912 <--				
WO 2002022572	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

GE, GH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
 LK, LR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 PH, PL, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
 UA, UG, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ,
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 CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2422055 A1 20020321 CA 2001-2422055
 20010912 <--
 AU 2001090873 A 20020326 AU 2001-90873
 20010912 <--
 EP 1318988 A2 20030618 EP 2001-970926
 20010912 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2004509103 T 20040325 JP 2002-526825
 20010912 <--
 AU 2001290873 B2 20060727 AU 2001-290873
 20010912 <--
 PRIORITY APPLN. INFO.: US 2000-231667P P
 20000911 <-- US 2001-273530P P
 20010305 <-- US 2001-298057P P
 20010613 <-- US 2000-273530P P
 20010305 <-- US 2000-298057P P
 20010613 <-- WO 2001-US28654 W
 20010912 <--
 OTHER SOURCE(S): MARPAT 136:263097
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. (4 Markush structures given), e.g., I [X = C(R3)2,
 O, SOO-2, NR2, NC(O)R7, NC(O)OR2, NS(O)2R7, C=O; Z = C(R3)2, C(O),
 O, NR, NC(O)OR, SOO-2; m = 1-5; n = 1-2; p = 0-2; q = 0-3; R = H,
 (cyclo)alkyl, (hetero)aryl, aralkyl, heteroaralkyl; R1 = H, alkyl,
 (hetero)aryl, aralkyl, heteroaralkyl; R, R1 may be connected
 through a covalent bond; R2 = H, alkyl, fluoroalkyl, aryl,
 heteroaryl, cycloalkyl; R3 = H, alkyl, aryl, OR2, OC(O)R2, CH2OR2,
 CO2R2; wherein any two instances of R3 may be connected by a
 covalent tether whose backbone consists of 1, 2, 3, or 4-carbon

atoms; R4 = H, alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, OR; R5-6 = H, alkyl, (CH2)qY, aryl, heteroaryl, F, OR2, OC(O)R2, or an instance of CR5R6 taken together is C(O); R7 = (cyclo)alkyl, (hetero)aryl, aralkyl, or heteroaralkyl; R8-9 = H, alkyl, (CH2)qY, (hetero)aryl, F, OR2, OC(O)R2, or an instance of CR8R9 taken together is C(O); Y = OR2, N(R2)2, SO0-2R2, P(O)(OR2)2; any two instances of R2 may be connected through a covalent bond; a covalent bond may connect R4 and an instance of R5 or R6; any two instances of R5 and R6 may be connected through a covalent bond; any two geminal or vicinal instances of R8 and R9 may be connected through a covalent bond; and the stereochem. configuration at any stereocenter of I is R, S or a mixture of these configurations.] were prepared Examples include synthesis of several hundred compds. of structure I, functional assays for norepinephrine (NE), dopamine (DA) and serotonin (5-HT) antagonism, determination of NE, DA and 5-HT reuptake inhibition, spontaneous locomotor activity/antidepressant behavioral assay in rats and the synthesis of a 96-member combinatorial library in which the library compds. were screened for monoamine uptake inhibition. For instance, 3-((4-trifluoromethylphenoxy)methyl)piperidine trifluoroacetate was alkylated with 1-[(4-chlorophenyl)cyclobutyl]-2-chloroethanone (preparation given) and the resulting product reduced with NaBH4 to give II. All 4 enantiomers of II were prepared by a stereospecific synthesis, and X-ray crystallog. determination of one enantiomer allowed the absolute stereochem. of III to be assigned. III had EC50 < 10 nM for DA reuptake inhibition compared to nomifensine = 11 nM. I are useful for the treatment of depression, sexual dysfunction, Alzheimer's disease, anxiety, etc.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L7 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:380438 CAPLUS Full-text

DOCUMENT NUMBER: 135:24657

TITLE: Selective cellular targeting: multifunctional delivery

vehicles

INVENTOR(S): Glazier, Arnold

PATENT ASSIGNEE(S): Drug Innovation & Design, Inc., USA

SOURCE: PCT Int. Appl., 981 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001036003	A2	20010525	WO 2000-US31262	

20001114 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH,

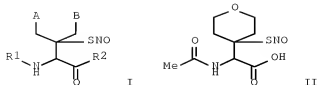
GM, HR,
 LS, LT,
 RO, RU,
 UZ, VN,
 YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
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 TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2391534 A1 20010525 CA 2000-2391534
 20001114 <--
 AU 2001016075 A 20010530 AU 2001-16075
 20001114 <--
 EP 1255567 A1 20021113 EP 2000-978631
 20001114 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 US 20030138432 A1 20030724 US 2000-738625
 20001215 <--
 PRIORITY APPLN. INFO.: US 1999-165485P P
 19991115 <--
 US 2000-239478P P
 20001011 <--
 US 2000-241937P P
 20001020 <--
 WO 2000-US31262 W
 20001114 <--
 US 2000-712465 B1
 20001115 <--
 AB The present invention relates to the compns., methods, and
 applications of a novel approach to selective cellular targeting.
 The purpose of this invention is to enable the selective delivery
 and/or selective activation of effector mols. to target cells for
 diagnostic or therapeutic purposes. The present invention relates
 to multi-functional prodrugs or targeting vehicles wherein each
 functionality is capable of enhancing targeting selectivity,
 affinity, intracellular transport, activation or detoxification.
 The present invention also relates to ultralow dose, multiple
 target, multiple drug chemotherapy and targeted immunotherapy for
 cancer treatment.

L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2000:535107 CAPLUS Full-text
 DOCUMENT NUMBER: 133:150471
 TITLE: Aromatic and heterocyclic S-nitrosothiols
 useful as agents for the treatment of circulatory
 dysfunctions
 INVENTOR(S): Repolles Moliner, Jose; Salas Perez-Rasilla,
 Eduardo;
 Pubill Coy, Francisco; Cerda Riudavets, Juan

Antonio;
 Lydia; Ferrer
 Banus,
 Llaguno,
 Pedro
 Lacer, S.A., Spain
 PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Spanish
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044714	A1	20000803	WO 2000-ES19	
20000119 <--				
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ES 2147162	A1	20000816	ES 1999-159	
19990127 <--				
ES 2147162	B1	20010316		
CA 2359027	A1	20000803	CA 2000-2359027	
20000119 <--				
CA 2359027	C	20081028		
BR 2000007395	A	20011030	BR 2000-7395	
20000119 <--				
EP 1157987	A1	20011128	EP 2000-900518	
20000119 <--				
EP 1157987	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102003	T2	20011221	TR 2001-2003	
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GB 2363604	A	20020102	GB 2001-20581	
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GB 2363604	B	20030910		
DE 10083902	T0	20020110	DE 2000-10083902	
20000119 <--				
HU 2001005203	A2	20020629	HU 2001-5203	

20000119 <--				
HU 2001005203	A3	20020828		
JP 2002535385	T	20021022	JP 2000-595971	
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JP 3795330	B2	20060712		
EE 200100389	A	20021216	EE 2001-389	
20000119 <--				
EE 4524	B1	20050815		
NZ 513162	A	20030131	NZ 2000-513162	
20000119 <--				
AU 764725	B2	20030828	AU 2000-30460	
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AT 249428	T	20030915	AT 2000-900518	
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PT 1157987	T	20040130	PT 2000-900518	
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ES 2206178	T3	20040516	ES 2000-900518	
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CN 1166631	C	20040915	CN 2000-803084	
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AP 1439	A	20050630	AP 2001-2247	
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IL 144381	A	20050831	IL 2000-144381	
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CZ 298871	B6	20080227	CZ 2001-2678	
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NO 2001003385	A	20010917	NO 2001-3385	
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IN 2001KN00742	A	20050311	IN 2001-KN742	
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US 20020058629	A1	20020516	US 2001-912164	
20010724 <--				
US 6800612	B2	20041005		
HR 2001000562	A1	20020831	HR 2001-562	
20010726 <--				
ZA 2001006182	A	20021028	ZA 2001-6182	
20010726 <--				
MX 2001007570	A	20030514	MX 2001-7570	
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BG 105824	A	20020628	BG 2001-105824	
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BG 64983	B1	20061130		
PRIORITY APPLN. INFO.:			ES 1999-159	A
19990127 <--				
			WO 2000-ES19	W
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OTHER SOURCE(S):	MARPAT	133:150471		
GI				



AB The invention relates to novel S-nitrosothiols derived from penicillamine or glutathione, of general formula I [wherein A, B = Ph; or AB = CH₂-Q-CH₂ where Q = O, S, or N-R₃; R₃ = H or C₁-C₄ alkyl; R₁ = C₁-C₅ aliphatic acyl or glutamic acid bonded by γ -carboxy group; R₂ = OH or glycine radical bonded by peptidic linkage so that R₂ = OH when R₁ = aliphatic acyl, and R₂ = glycine when R₁ = glutamic acid]. The compds. exhibit vasodilating and blood platelet aggregation-inhibiting activity, and are useful in the treatment of circulatory system dysfunctions, especially cardiovascular dysfunctions. For instance, 2-amino-2-(4-mercaptotetrahydropyran-4-yl)acetic acid HCl salt was neutralized with NaOH and then N-acetylated with AcCl in MeCN, and the N-acetyl derivative was S-nitrosylated with HCl and NaNO₂ in aqueous MeOH under sonication, to give invention compound II. In an in vitro assay for vasodilation of norepinephrine-contracted arterial rings, II had an EC₅₀ of 0.375 μ M, vs. 1.56 μ M for the known comparison compound S-nitrosoglutathione, and 0.024-1.89 μ M for other invention compds. I.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l5 and (vasomotor? or vasodilat? or menopaus? or flash? or flush? or sweat?)

6995 L5
4817 VASOMOTOR?
49919 VASODILAT?
20783 MENOPAUS?
76912 FLASH?
26045 FLUSH?
10530 SWEAT?

L8 89 L5 AND (VASOMOTOR? OR VASODILAT? OR MENOPAUS? OR FLASH? OR FLUSH
? OR SWEAT?)

=> s l8 and (py<2003 or ay<2003 or pry<2003)
22983475 PY<2003
4504208 AY<2003
3973137 PRY<2003

L9 24 L8 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d 19 ibib abs 1-10

L9 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

DOCUMENT NUMBER: 144:57525
 TITLE: Coated vaginal devices for vaginal delivery of
 therapeutically effective and/or health-
 promoting agents
 INVENTOR(S): Wilson, Michelle; Desai, Kishorkumar J.;
 Pauletti, Giovanni M.; Antoon, Mitchell K.; Clendening,
 Chris E.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part
 of U.S. Ser. No. 126,863
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 12
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050276836	A1	20051215	US 2005-180076	
20050712 <--				
US 6197327	B1	20010306	US 1998-79897	
19980515 <--				
US 6086909	A	20000711	US 1999-249963	
19990212 <--				
US 6572874	B1	20030603	US 2000-626025	
20000727 <--				
NZ 508130	A	20020301	NZ 2000-508130	
20001113 <--				
AU 765269	B2	20030911	AU 2001-54192	
20010703 <--				
US 20030049302	A1	20030313	US 2002-226667	
20020821 <--				
US 6982091	B2	20060103		
US 20040005345	A1	20040108	US 2003-349029	
20030122 <--				
US 6905701	B2	20050614		
US 20040043071	A1	20040304	US 2003-600849	
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US 20050249774	A1	20051110	US 2005-126863	
20050510 <--				
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			US 1998-79897	A2
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			US 1999-249963	A2
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			US 2000-626025	A2
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			US 2002-226667	A2
20020821 <--				
			US 2003-349029	A2
20030122				
			US 2003-600849	A2

20030620	US 2004-587454P	P
20040712	US 2005-126863	A2
20050510	AU 1998-76976	A3
19980610 <--	NZ 1998-502120	A1
19980610 <--	US 1999-146218P	P
19990728 <--	US 2001-315877P	P
20010829 <--	US 2002-390748P	P

20020621 <--

AB Disclosed is a vaginal device for delivering therapeutical and/or health-promoting agents. The vaginal device partly or completely coated by, covered by or combined with a coating or covering comprising a film, foam, strip, cap, cup or particles. The coating of the device comprises a mucoadhesive composition comprising a therapeutical and/or health-promoting agent. For example, sumatriptan vaginal suppository were prepared from Suppocire AS2X, hydroxypropyl Me cellulose as a mucoadhesive agent, and Transcutol as a permeation enhancer.

L9 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2005:326539 CAPLUS Full-text

DOCUMENT NUMBER: 142:355418

TITLE: An improved process for the preparation of
(-)-3-carene-5-one from (+)-3-carene by

air/oxygen

INVENTOR(S): oxidation
Khullar, Alok; Pandey, Inder Kumar; Sharma,
Rajeev

Kumar; Sharma, Sudhir Kumar; Shrivastava,

Dhananjay;

PATENT ASSIGNEE(S): Madhusoodanan, S.; Rajaram
SOURCE: Montari Industries Ltd., India
Indian, 20 pp.

CODEN: INXXAP

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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IN 188755	A1	20021102	IN 1998-DE1628	
19980612 <--				
PRIORITY APPLN. INFO.:			IN 1998-DE1628	
19980612 <--				
OTHER SOURCE(S):			CASREACT 142:355418; MARPAT 142:355418	
GI				



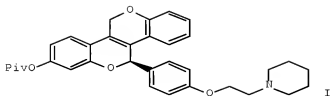
AB This invention relates to an improved process for the preparation of (-)-3-carene-5-one (I) from (+)-3-carene (II) by air/oxygen oxidation comprising: (1) charging II under pos. air/oxygen pressure into the reactor (as shown in figure I), with or without a solvent; (2) increasing the air/oxygen flow to 60-200 LPH per Kg of II; (3) charging the catalyst, MR1R2X1X2 [M = cobalt; R1,R2 = pyridine; X1, X2 = halogen (especially Cl, Br)] as herein described at 0.1-15% weight II; (4) heating the reaction mass to 40-100°C; (5) maintaining the reaction mass at 40-100°C for 6-32 h; (6) cooling the reaction mass to 30°C; (7) filtering off the solids through a celite bed; (8) flash distilling the crude mass through a falling film evaporator, (FFE), as shown in Figure II, under reduced pressure. To continue: (9) fractionating the distillate through an efficient fractionating column at very low pressure (as shown in Figure II): (10) collecting I of 50-60% purity at the bottom; (11) collecting II at the top along with other low boiling compds.; (12) passing the I of step 10 once again through the assembly, as shown in figure II, to get 70-80% pure product, under reduced pressure.

L9 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:1127099 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 142:56279
 TITLE: Preparation of tetracyclic heterocycles as selective estrogen receptor modulators (SERMs).
 INVENTOR(S): Kanojia, Ramesh M.; Jain, Nareshkumar F.; Ng, Raymond;
 Sui, Zhihua; Xu, Jiayi
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 110 pp., Cont.-in-part of U.S. Ser. No. 307,735.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040259915	A1	20041223	US 2003-719875	

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US 7105679 B2 20060912
 US 20030216463 A1 20031120 US 2002-307735
 20021202 <--
 US 7329654 B2 20080212
 CA 2505857 A1 20040617 CA 2003-2505857
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 WO 2004050660 A1 20040617 WO 2003-US37419
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 20031121 <--
 JP 2006514941 T 20060518 JP 2004-557261
 20031121 <--
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 20031121 <--
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 20031121 <--
 MX 2005005897 A 20060208 MX 2005-5897
 20050602 <--
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 PRIORITY APPLN. INFO.: US 2001-341957P P
 20011219 <-- US 2002-307735 A2
 20021202 <-- WO 2003-US37419 W
 20031121
 OTHER SOURCE(S): CASREACT 142:56279
 GI



AB There are 5 claimed compds., e.g., I and over 100 synthetic examples of selective estrogen receptor modulators. Thus, 3-(2-hydroxy-4-methoxyphenyl)-7-hydroxy-4-methylchromen-2-one (preparation given), in methanol/acetone was added at room temperature anhydrous potassium carbonate; the solution was stirred 2 h to give 2,8-dihydroxy-1H-chromeno[4,3-c]chromen-5-one. The latter bound to estrogen α and β receptors at 0.505 μ M and 0.061 μ M, resp. I are useful in the treatment and/or prevention of disorders associated with the depletion of estrogen such as hot flashes, vaginal dryness, osteopenia and osteoporosis; hormone sensitive cancers and hyperplasia of the breast, endometrium, cervix and prostate; endometriosis, uterine fibroids, osteoarthritis and as contraceptive agents, alone or in combination with a proestrogen or proestrogen antagonist.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:681641 CAPLUS Full-text

DOCUMENT NUMBER: 141:185589

TITLE: Methods for restoring functionality of

gonadotropin

releasing hormone receptor mutants with

indoles,

quinolones and macrolides derivatives and

therapeutic

uses thereof

INVENTOR(S): Conn, P. Michael

PATENT ASSIGNEE(S): Oregon Health and Science University, USA

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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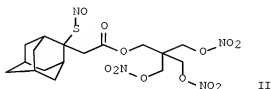
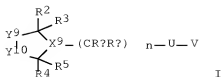
WO 2004069859 A2 20040819 WO 2004-US2290
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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
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GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2004208990 A1 20040819 AU 2004-208990
20040127 CA 2514449 A1 20040819 CA 2004-2514449
20040127 EP 1599494 A2 20051130 EP 2004-705679
20040127 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 20050203019 A1 20050915 US 2005-50662
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PRIORITY APPLN. INFO.: US 2003-443691P P
20030129 US 2001-328319P P
20011009 <-- US 2002-376685P P
20020429 <-- WO 2002-US32399 W
20021008 <-- WO 2004-US2290 W
20040127 US 2004-492295 A2
20040408
AB Methods are disclosed for screening for agents that can at least
partially restore function to several mutant gonadotropin
releasing hormone receptors (GnRHRs), which can increase cell-
surface expression of wild-type GnRHR, or both. In addition,
methods are provided for using the identified agents for treating
subjects having hypogonadism.

L9 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2009 ACS ON STN
ACCESSION NUMBER: 2003:836762 CAPLUS Full-text
DOCUMENT NUMBER: 139:350474
TITLE: Preparation and compositions of nitrosothio
(hetero)cyclic nitric oxide donors
INVENTOR(S): Fang, Xinqin; Garvey, David S.; Gaston, Ricky
D.; Lin, Chia-en; Ranatunga, Ramani R.; Richardson,
Stewart K.; Wang, Tiansheng; Wang, Weiheng; Wey, Shioh-ji
PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 138 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086282	A2	20031023	WO 2003-US10562	
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WO 2003086282	A3	20040429		
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20020405 <--			WO 2003-US10562	W
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OTHER SOURCE(S):	MARPAT	139:350474		
GI				



AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO2; X9 = CR10 or N; Y9 = CR6R7, NRi, NR25, NRiCR6R7, CR6R7NRi, CR2R3CR6R7, or CR6R7CR2R3; Y10 = CR8R9 or CR8R9CR17R18; R2-R9, R17, and R18 = independently H or alkyl; or R2R3, R4R5, R6R7, or R8R9 = independently oxo; or R4 and R7 together with the C's to which they are attached = cycloalkyl; or CR6R7 = cycloalkyl; R6 and R9 taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R7 and R8 are not present; R4 and R25 taken together with the C and N to which they are attached = heterocyclyl; Ra = lone pair of electrons, H, or (aryl)alkyl; Re and Rf = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CR6Rf = heterocyclyl or (bridged) cycloalkyl; Ri = H or (un)substituted alkyl, aryl, carboxamido, sulfonamido, etc.; n = 0-3; and pharmaceutically acceptable salts thereof] were prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiolo. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH2Cl2 to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC50 of 5 μM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight inhibition, or exhibited much higher IC50 values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting

wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:717760 CAPLUS Full-text

DOCUMENT NUMBER: 139:245903

TITLE: Preparation of [(hetero)arylsulfonylamino]-[1-substituted-piperidin-4-

yl]-acetic acids as metalloprotease inhibitors
Pikul, Stanislaw; Ohler, Norman Eugene;

INVENTOR(S): Almstead, Neil

Gregory; Laughlin, Steven Karl; Natchus,

Michael

George; De, Biswanath

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part

of Appl.

PCT/US01/08783.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

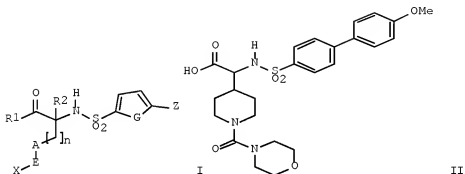
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030171400	A1	20030911	US 2002-246201	
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WO 2001070690	A1	20010927	WO 2001-US8783	
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
20000321 <--

US 2000-191303P P
WO 2001-US8783 A2

20010320 <--
OTHER SOURCE(S): MARPAT 139:245903
GI



AB The title compds. [I; R1 = OH, NHOH; R2 = H, alkyl, haloalkyl, etc.; A = (un)substituted monocyclic heterocycloalkyl; A can be connected to R2 to form (un)substituted monocyclic heterocycloalkyl; n = 0-4; E = a bond, alkyl, CO, etc.; X = H, alkyl, aryl, etc.; G = S, O, N:N, etc.; Z = cycloalkyl, heterocycloalkyl, etc.] such as II which are inhibitors of metalloproteases and which are effective in treating conditions characterized by excess activity of these enzymes such as arthritis and cancer, were claimed and formulated (prepn. are given but no data are given for intermediates and final compds.).

L9 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:511339 CAPLUS [Full-text](#)
DOCUMENT NUMBER: 139:85328
TITLE: Preparation of tetracyclic heterocycles as
selective estrogen receptor modulators (SERMs).
INVENTOR(S): Kanojia, Ramesh M.; Jain, Nareshkumar F.; Ng,
Raymond;
Sui, Zhihua; Xu, Jiayi
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

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CA 2471107 A1 20030703 CA 2002-2471107
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BR 2002015152 A 20041019 BR 2002-15152
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EP 1467998 A1 20041020 EP 2002-797167
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20021202 <--
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RU 2305099 C2 20070827 RU 2004-118606
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20040616 <--
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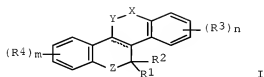
WO 2002-US38486 W

20021202 <--

OTHER SOURCE(S):

MARPAT 139:85328

GI



AB Title compds. [I; dotted line = optional double bond; X = O, S, CRaRb, CO; Y = CRaRb, CRaRb(CRaRb)1-2, CRaRbCO, CRaRbCOCRaRb, CO, O, S; Z = O, S; R1 = H, (substituted) alkyl, alkenyl, cycloalkyl, aryl, aroyl, aralkyl, heteroaryl, heteroarylalkyl; R2 = OH, (substituted) alkyl, alkenyl, cycloalkyl, aryl, aroyl, aralkyl, heteroaryl, heteroarylalkyl; R1R2 = O; m, n = 0-4; R3, R4 = halo, OH, amino, NO2, cyano, CORg, CO2Rg, etc.; Rg = H, alkyl, aryl, aralkyl, 1,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan-3-one; with provisos], were prepared. Thus, 3-(2-hydroxy-4-methoxyphenyl)-7-hydroxy-4-methylchromen-2-one (preparation given), in methanol/acetone was added at room temperature anhydrous potassium carbonate; the solution was stirred 2 h to give 2,8-dihydroxy-1H-chromeno[4,3-c]chromen-5-one. The latter bound to estrogen α and β receptors at 0.505 μ M and 0.061 μ M, resp. I are useful in the treatment and/or prevention of disorders associated with the depletion of estrogen such as hot flashes, vaginal dryness, osteopenia and osteoporosis; hormone sensitive cancers and hyperplasia of the breast, endometrium, cervix and prostate; endometriosis, uterine fibroids, osteoarthritis and as contraceptive agents, alone or in combination with a progestogen or progestogen antagonist.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2002:849626 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 137:370083

TITLE: Preparation of pyrazolo[1,5-a]pyridines as antagonists

of corticotropin-releasing factor receptor and medicines containing the same

INVENTOR(S): Hibi, Shigeki; Kikuchi, Koichi; Hoshino, Yorihiisa;

Soejima, Motohiro; Yoshiuchi, Tatsuya; Shin,

Kogyoku;

Ono, Mutsuko; Takahashi, Yoshinori; Shibata,

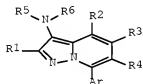
Hisashi;

Ino, Mitsuhiro; Hirakawa, Tetsuya

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 240 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088121	A1	20021107	WO 2002-JP4173	
20020425 <--				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
BE, CH, SE, TR, TD, TG				
CA 2443802	A1	20021107	CA 2002-2443802	
20020425 <--				
AU 2002251546	A1	20021111	AU 2002-251546	
20020425 <--				
AU 2002251546	B2	20070118		
EP 1389618	A1	20040218	EP 2002-720608	
20020425 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1505630	A	20040616	CN 2002-808872	
20020425 <--				
CN 1290846	C	20061220		
BR 2002009252	A	20040720	BR 2002-9252	
20020425 <--				
HU 2004001292	A2	20041228	HU 2004-1292	
20020425 <--				
NZ 529333	A	20050128	NZ 2002-529333	
20020425 <--				
RU 2308457	C2	20071020	RU 2003-134371	
20020425 <--				
JP 4206273	B2	20090107	JP 2002-585420	
20020425 <--				
MX 2003009738	A	20040129	MX 2003-9738	
20031023 <--				
NO 2003004788	A	20031229	NO 2003-4788	
20031024 <--				

KR 881647	B1	20090204	KR 2003-713949	
20031024 <--				
US 20040122039	A1	20040624	US 2003-250693	
20031027 <--				
US 7091215	B2	20060815		
ZA 2003008860	A	20050214	ZA 2003-8860	
20031113 <--				
US 20060217348	A1	20060928	US 2006-446416	
20060605 <--				
US 7285666	B2	20071023		
IN 2007CN01966	A	20070831	IN 2007-CN1966	
20070508 <--				
US 20070249663	A1	20071025	US 2007-757595	
20070604 <--				
KR 2008031501	A	20080408	KR 2008-705209	
20080229 <--				
KR 876622	B1	20081231		
PRIORITY APPLN. INFO.:			JP 2001-133207	A
20010427 <--				
			IN 2003-DN1748	A3
20020425 <--				
			WO 2002-JP4173	W
20020425 <--				
			KR 2003-713949	A3
20031024				
			US 2003-250693	A3
20031027				
			US 2006-446416	A3
20060605				
OTHER SOURCE(S):		MARPAT 137:370083		
GI				



I

AB Compds. represented by the general formula (I), salts thereof, and hydrates of both [wherein R1 = H, halo, NO2, cyano, -G1-R1a (wherein G1 = CH2, O, S, SO, SO2, CO, CO2, O2C, NR1b, CONR1b, SO2NR1b, NR1bCO, NR1bSO2; R1a, R1b = H, C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-8 cycloalkyl, C5-8 cycloalkenyl); R2, R3, R4 = H, halo, cyano, NO2, HO, C6-14 aryl, 5- to 14-membered heteroaryl, G2-R2a (wherein G2 = a single bond, C1-6 alkylene, O, S, SO, SO2, CO, CO2, O2C, NR2b, CONR2b, SO2NR2b, NR2bCO, NR2bSO2; R2a, R2b = H, optionally 1-3 of halogen-substituted C1-6 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-8 cycloalkyl, C5-8 cycloalkenyl), etc.; R5, R6 = -X5-X6-X7 (wherein X5 = a single bond, CO; X6 = a single bond, NR3a, O, S, SO, SO2, C1-10 alkylene, C2-10 alkenylene, C2-10 alkynylene; X7, R3a = H, C1-10 alkyl, C2-10

alkenyl, C2-10 alkynyl, C3-8 cycloalkyl, C5-8 cycloalkenyl, C6-14 aryl, etc.); or R5 and R6 are linked together to form a 5- to 7-membered ring optionally containing 1-4 heteroatoms or CO in the ring; or R6 and R2 are linked together to form a 6- or 7-membered ring optionally containing 1 or 2 heteroatoms or CO in the ring; Ar = C6-14 aryl, 5- to 14-membered heteroaryl, 9- to 11-membered benzene-fused cyclic group, 8- to 11-membered heteroaryl-fused cyclic group] are prepared. These compds. are antagonists of corticotropin-releasing factor (CRF) receptor, in particular CRF 1 or 2 receptor, and useful for the treatment or prevention of CRF-related diseases. The above diseases include depression, symptom of depression, mania, anxiety, general anxiety disorder, panic disorder, phobia, obsessive-compulsive disorder, post-traumatic-stress disorder, Tourette's syndrome, autism, emotional disorder, emotional disturbance, bipolar disorder, cyclothymia, schizophrenia, peptic ulcer, irritable bowel syndrome, ulcerous colitis, Crohn's disease, diarrhea, constipation, ileus after surgery, gastrointestinal disorder accompanied by stress, or neural vomiting. They also include Alzheimer's disease, Alzheimer's-type senile dementia, neurodegenerative disease, multiple infarctional dementia, senile dementia, neural anorexia, eating disorder, obesity, diabetes, alc. dependency (alcoholism), drug preference, drug withdrawal symptom, alc. withdrawal symptom, sleep disorder, insomnia, migraine headache, stress headache, myotonic headache, ischemic nerve disorder, excitatory toxin-induced nerve disorder, cerebral apoplexy, progressive supranuclear paralysis, amyotrophic lateral sclerosis, multiple sclerosis, muscle spasm, chronic fatigue syndrome, psychosocial growth-retardation, epilepsy, and head trauma. Addnl. included are spinal cord injury, writer's cramp, torticollis spastica, cervicobrachial syndrome (cervix-shoulder arm symptom), primary glaucoma, Meniere's disease, vegetative dystonia, alopecia, neuropathy, hypertension, cardiovascular diseases, tachycardia, congestive heart paralysis, hyperpnea syndrome, bronchial asthma, apnea syndrome, infant sudden death syndrome, inflammation disorder, pain, allergy, impotence, menopausal syndrome, fertilization disorder, sterility, cancer, immune function abnormality in HIV infection or stress, hemorrhagic shock, Cushing syndrome, thyroid gland malfunction, meningitis, acromegaly, incontinence, or osteoporosis. The above symptom of depression includes major, single episode, or recurrent depression, child abuse due to depression, or postpartum depression. Thus, 5 mg 7-(2-chloro-4-methoxyphenyl)-2-ethyl-3-nitropyrzazolo[1,5-*a*]pyridine was suspended in 2 mL ethanol, followed by adding 1 mL H₂O, 0.5 mL AcOH, and 10 mg Zn, and the resulting mixture was stirred at 80° for 30 min to give crude 7-(2-chloro-4-methoxyphenyl)-2-ethylpyrazolo[1,5-*a*]pyridin-3-ylamine (II). II was dissolved in 1 mL THF and treated with 0.015 mL propionaldehyde and 0.071 mL 3 M aqueous H₂SO₄, followed by adding 5.4 mg NaBH₄ in five portions with vigorous stirring under ice-cooling, and the resulting mixture was stirred for 30 min to give 6 mg N-[7-(2-chloro-4-methoxyphenyl)-2-ethylpyrazolo[1,5-*a*]pyridin-3-yl]-N,N-dipropylamine (III). III showed IC₅₀ of 50 nM for inhibiting the binding of [125I]-Savagine on a membrane preparation from HEK293 cell expressing human CRF receptor 1.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:846387 CAPLUS Full-text
 DOCUMENT NUMBER: 138:221163
 TITLE: Novel generation of an o-quinone methide from
 2-(2'-cyclohexenyl)phenol by excited state
 intramolecular proton transfer and subsequent

C-C

fragmentation
 AUTHOR(S): Delgado, Julio; Espinos, Amparo; Consuelo
 Jimenez, M.;
 CORPORATE SOURCE: Miranda, Miguel A.
 Departamento de Quimica, Instituto de
 Tecnologia
 Quimica UPV-CSIC, Valencia, 46071, Spain
 SOURCE: Chemical Communications (Cambridge, United
 Kingdom) (

2002), (22), 2636-2637
 CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Formation of an o-quinone methide via C-C fragmentation of a
 zwitterion formed by intramol. excited state proton transfer from
 an o-allylphenol derivative is reported for the first time.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE
 FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

=> d l9 ibib abs 11-24

L9 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:575071 CAPLUS Full-text
 DOCUMENT NUMBER: 137:140382
 TITLE: Preparation of 2H-1-benzopyran derivatives for
 the

prevention and treatment of postmenopausal

pathologies

INVENTOR(S): Delcanale, Maurizio; Amari, Gabriele; Armani,
 Elisabetta; Civelli, Maurizio; Galbiati,

Elisabetta

PATENT ASSIGNEE(S): Chiesi Farmaceutici S.P.A., Italy

SOURCE: PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002059113	A1	20020801	WO 2002-EP567	

20020121 <--
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
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 GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
 OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,
 TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,
 BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
 SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
 TD, TG
 EP 1229036 A1 20020807 EP 2001-101521
 20010124 <--
 EP 1229036 B1 20050112
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
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 AT 286893 T 20050115 AT 2001-101521
 20010124 <--
 ES 2236056 T3 20050716 ES 2001-101521
 20010124 <--
 EP 1281710 A1 20030205 EP 2001-118682
 20010803 <--
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 CA 2435775 A1 20020801 CA 2002-2435775
 20020121 <--
 AU 2002237282 A1 20020806 AU 2002-237282
 20020121 <--
 AU 2002237282 B2 20070215
 EP 1355906 A1 20031029 EP 2002-703564
 20020121 <--
 EP 1355906 B1 20050112
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 BR 2002007066 A 20040330 BR 2002-7066
 20020121 <--
 JP 2004517151 T 20040610 JP 2002-559415
 20020121 <--
 ZA 2003005684 A 20040723 ZA 2003-5684
 20020121 <--
 HU 2004001018 A2 20040928 HU 2004-1018
 20020121 <--
 HU 2004001018 A3 20070529
 AT 286894 T 20050115 AT 2002-703564
 20020121 <--
 NZ 527144 A 20050324 NZ 2002-527144
 20020121 <--

PT 1355906	T	20050531	PT 2002-703564	
20020121 <--				
ES 2236485	T3	20050716	ES 2002-703564	
20020121 <--				
CN 1261431	C	20060628	CN 2002-804066	
20020121 <--				
MX 2003006505	A	20040421	MX 2003-6505	
20030721 <--				
NO 2003003318	A	20030924	NO 2003-3318	
20030723 <--				
US 20040106595	A1	20040603	US 2003-466118	
20031222 <--				
US 6951883	B2	20051004		
HK 1060558	A1	20050513	HK 2004-102904	
20040426 <--				
PRIORITY APPLN. INFO.:			EP 2001-101521	A
20010124 <--				
			EP 2001-118682	A
20010803 <--				
			WO 2002-EP567	W
20020121 <--				
OTHER SOURCE(S):	MARPAT 137:140382			
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB The title compds. [I; R1, R2 = H, alkyl, haloalkyl, alkenyl, haloalkenyl; or NR1R2 = 4-8 membered heterocyclyl; X = H, alkyl, aryl, NO2, halo, OR3 (R3 = H, alkyl, aryl, alkanoyl, aryloyl); X1 = H, alkyl, alkoxy; and X and X1 can form, together with the carbon atoms they are bound to, a fused aromatic ring to give an α -naphthalenyl; Y = H, alkyl, alkanoyl, aryloyl, alkylaminocarbonyl, alkylloxycarbonyl; Z = H, OR4 (R4 = H, alkyl, alkanoyl, aryloyl); m = 1-2; n = 0-1; p = 2-6] and their pharmaceutically acceptable salts, useful for the prevention and treatment of postmenopausal pathologies, were prepared E.g., a multi-step synthesis of II.HCl, starting from formononetin, which showed binding K_i of 0.017 ± 0.002 nM and 0.099 ± 0.005 nM against human estrogen receptor ER- α and ER- β , resp, was given.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE
FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:411178 CAPLUS [Full-text](#)
DOCUMENT NUMBER: 137:362766
TITLE: Dipeptide sulfonamides as endothelin ETA/ETB
receptor
antagonists
AUTHOR(S): Ksander, Gary M.; Shetty, Suraj S.; DelGrande,
Dominick; Balwierczak, Joseph L.; Bruseo,

Charles W.; Savage, Paula; DeJesus, Reynalda; Yuan,
 Andrew; Webb, Randy L.; Jeng, Arco Y.
 CORPORATE SOURCE: Metabolic and Cardiovascular Diseases
 Research, Novartis Institute for Biomedical Research,
 Summit, NJ, 07901, USA
 SOURCE: Canadian Journal of Physiology and
 Pharmacology (2002), 80(5), 464-469
 CODEN: CJPPA3; ISSN: 0008-4212
 PUBLISHER: National Research Council of Canada
 DOCUMENT TYPE: Journal
 LANGUAGE: English

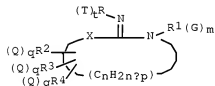
AB Endothelin-1 (ET-1) is a potent mitogen and modulator of vascular
 tone. It is synthesized and released from endothelial cells and
 acts upon two receptor subtypes designated as ETA and ETB. In
 this study, a series of potent dipeptide sulfonamide dual-
 endothelin ETA/ETB receptor antagonists were prepared to
 investigate their potential benefit in vascular diseases. CGS
 31398 inhibited [125I]ET-1 binding to human ETA and ETB receptors
 expressed in Chinese hamster ovary (CHO) cells (ETA/CHO, ETB/CHO)
 with resp. IC50 values of 0.26 and 0.12 nM. However, in
 anesthetized rats, this compound markedly potentiated ET-1-induced
 renal vascular resistance, a response normally observed with
 selective ETB receptor antagonists. To determine whether species
 differences account for these results, a direct comparison was
 made between binding to rat and rabbit aortic membranes vs.
 functional antagonism in isolated rat aortic rings. It was found
 that CGS 31398 had potent affinity for the ETA receptor in rat and
 rabbit aorta with IC50 values of 0.87 and 0.79 nM, resp.
 Inhibition of ET-1-induced contractions of rat aorta by the
 compound was considerably weaker than expected (pKB = 6.4), while
 that of sarafotoxin S6c induced contraction of dog saphenous vein
 (100% inhibition at 100 nM) was consistent with corresponding
 binding data. These results suggest that although CGS 31398 is a
 potent dual inhibitor of ETA/ETB receptor binding, it surprisingly
 displays potent ETB and weak ETA receptor antagonism in functional
 assays.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

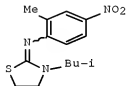
L9 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:165042 CAPLUS Full-text
 DOCUMENT NUMBER: 136:216746
 TITLE: Preparation and use of, e.g.,
 2-arylimino-1,3-thiazolidines as progesterone
 receptor binding ligands
 INVENTOR(S): Dixon, Brian R.; Bagi, Cedo M.; Brennan,
 Catherine R.; Brittelli, David R.; Bullock, William H.;
 Chen,

Johnson, Jinshan; Collibee, William L.; Dally, Robert;
 William Jeffrey S.; Kluender, Harold C. E.; Lathrop,
 Aniko M.; F.; Liu, Peiying; Mase, Carol Ann; Redman,
 Donald J. Scott, William J.; Urbahns, Klaus; Wolanin,
 PATENT ASSIGNEE(S): Bayer Corp., USA
 SOURCE: U.S., 148 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6353006	B1	20020305	US 1999-453613	
19991203 <--				
US 20030207865	A1	20031106	US 2001-4306	
20011023 <--				
PRIORITY APPLN. INFO.:			US 1999-287573P	P
19990114 <--				
			US 1999-453613	A3
19991203 <--				
OTHER SOURCE(S):	MARPAT	136:216746		
GI				



I



II

AB Title compds. I [R = substituted Ph, wherein the substituent is selected from T or substituted pyridyl; R1 = (cyclo)alkyl, (cyclo)alkenyl, alkynyl; R2-4 = H, (cyclo)alkyl, (cyclo)alkenyl, oxo, representing two of the groups R2-4; X = S(O)0-2; n = 2; p = sum of non-H substituents R2-4; T = alk(en/yn)yl, alkoxy, NO2, CN, halo; t = 1-5, provided that when T = alk(en/yn)yl, alkoxy, T is optionally substituted; G = halo, alkoxy, (cyclo)alk(en)yl, aryl, CN; q = 0-4, with the exception of halogen, which may be employed up to the perhalo level provided that when substituent G is alkyl, alkenyl, etc. then G is optionally substituted; Q = of (halo)alkyl, cycloalkyl, alkoxy, alkenyl, cycloalkenyl, etc.; q = 0-4; with some provisions] were prepared E.g. 2-chloroethylammonium chloride was reacted with (2-methyl-4-nitrophenyl)isothiocyanate (CH2Cl2, Et3N) to give the thiazolidine which was alkylated with i-Bu bromide (DMF, Cs2CO3, 90°C) to give

II. Most compds. of the invention at 200 nM caused at least 30% inhibition of progesterone while, e.g., II caused >80% inhibition at the same concentration I are useful in the treatment of luteal deficiency, osteoporosis, hirsutism, etc.

REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN

THE RE

FORMAT

L9 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:51274 CAPLUS Full-text

DOCUMENT NUMBER: 136:96100

TITLE: Use of dammarane-type triterpenoid saponins

INVENTOR(S): Raj Kumar, Chinni Krishnan

PATENT ASSIGNEE(S): Raj Kumar, Sujatha, India; Argaet, Victor

Peter

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003996	A1	20020117	WO 2001-AU837	
20010712 <--				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 2003CN00260	A	20050408	IN 2003-CN260	
20030213 <--				
PRIORITY APPLN. INFO.:			AU 2000-8750	A
20000712 <--			AU 2000-1146	A
20001031 <--			WO 2001-AU837	W
20010712 <--				

OTHER SOURCE(S): MARPAT 136:96100

AB The present invention discloses the use of a dammarane-type triterpenoid saponin or derivative or pharmaceutically acceptable salt thereof for treating or preventing conditions, which are

related to reduced nitric oxide levels, or which are ameliorable or preventable by augmentation of nitric oxide levels, within the human body, or for promoting responses requiring enhanced nitric oxide levels within the human body. A saponin extract obtained from *Bacopa monnieri* is shown to induce vascular nitric oxide production in rabbit aorta rings, to enhance growth of human neuroblastoma cells (neuronal filament formation), to reduce expression of amyloid precursor protein in HeLa cells transfected with the APP, to prevent leg cramps and decrease involuntary muscle movements in a patient, to cure chilblains in another patient, and to enhance the quantity and quality (protein and vitamin level) of milk in Jersey cows.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:827173 CAPLUS Full-text

DOCUMENT NUMBER: 136:147406

TITLE: Combination of chromatographic and spectroscopic

methods for the isolation and characterization

of

polar guaianolides from *Achillea asiatica* Glasl, Sabine; Gunbilig, Disan; Narantuya,

AUTHOR(S): Samdan;

Werner, Ingrid; Jurenitsch, Johann

CORPORATE SOURCE: Pharmacognosy,

Centre of Pharmacy, Institute of

University of Vienna, Vienna, A-1090, Austria

SOURCE: Journal of Chromatography, A (2001), 936(1-2), 193-200

CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Four polar guaianolides, 8 α -angeloxy-2 α ,4 α ,10 β - trihydroxy-6 β H,7 α H,11 β H-1(5)-guaien-12,6 α -olide; 8 α -angeloxy-1 β ,2 β :4 β ,5 β -diepoxy-10 β -hydroxy- 6 β H,7 α H,11 β H-12,6 α -guaianolide; 8 α -angeloxy-4 α ,10 β -dihydroxy-2-oxo-6 β H, 7 α H, 11 β H-1(5)-guaien-12,6 α -olide and 8-desacetyl-matricarin, were isolated from *Achillea asiatica* and characterized by TLC, MS, IR, HPLC and diode array detection. Purified exts. were separated by means of flash chromatog. HPLC seps. were achieved using different methanol-water gradients as mobile phase and LiChrospher 100-RP8 5 μ m or Zorbax SB-C8 3.5 μ m as stationary phases. The chromatog. data are compared to those of the proazulene 8 α -tigloxy-artabsin which shows antiinflammatory effects. By means of these characteristics the identification of the guaianolides with potential antiphlogistic properties is also possible from other sources.

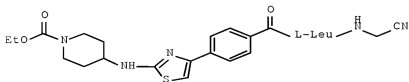
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:693319 CAPLUS Full-text
 DOCUMENT NUMBER: 135:257468
 TITLE: Preparation of
 N-(4-thiazolylbenzoyl)-N-(cyanomethyl)-L-
 leucinamides
 and analogs as protease inhibitors
 INVENTOR(S): Palmer, James T.; Setti, Eduardo L.; Tian,
 Zong-Qiang;
 Venkatraman, Shankar; Wang, Dan-Xiong
 PATENT ASSIGNEE(S): Axy's Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 73 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001068645	A2	20010920	WO 2001-US8332	
20010314 <--				
WO 2001068645	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-189694P	P
20000315 <--				
GI				



AB The title compds. and their pharmaceutically acceptable salts, N-oxides, prodrugs, protected derivs., or isomers thereof were prepared as cysteine protease inhibitors. For example, stirring a solution of 4-[2-(1-tert-butoxycarbonylpiperidin-4-ylamino)thiazol-4-yl]benzoic acid (preparation given) and the MeSO₃H salt of 2S-amino-N-cyanomethyl-4-methylpentanamide overnight at room temperature with PyBOP and diisopropylethylamine in DMF, followed by conversion to the Et ester, yielded I (77%). Test compds. inhibited cathepsin B, K, L, and S (no data). The invention compds. and compns. with a bisphosphonic acid and/or an estrogen receptor agonist are claimed for treating osteoporosis in post-menopausal women (no data).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:624328 CAPLUS Full-text

DOCUMENT NUMBER: 135:185445

TITLE: Triterpene compositions for hormonal disorder treatment

INVENTOR(S): Chen, Dihua; Si, Jianyong; Zhao, Xiaohong; Shen,

Liangang

PATENT ASSIGNEE(S): Shandong Luye Pharmaceutical Co., Ltd., Peop. Rep.

China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp.

CODEN: CNXXEV

DOCUMENT TYPE:

Patent

LANGUAGE:

Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CN 1281698	A	20010131	CN 1999-111106	
19990723 <--				
CN 1099287	C	20030122		
PRIORITY APPLN. INFO.:			CN 1999-111106	
19990723 <--				

AB The medicinal composition is composed of cimicifugoside H-2 15-25, cimicifugoside H-1 12-22, 7,8-didehydro-27-deoxyshengmating 5-15, 27-deoxyshengmating 5-15, shengmating 1-10, shengmacichun dixyloside 1-10, 7,8-didehydrocimigenol O-xyloside 1-5, and 24-oxoacetyl cimigenol O-xyloside 1-5 part. The medicinal composition increases the serum level of estradiol and decreases the serum level of FSH and may be used for treatment of menopausal osteoporosis.

L9 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

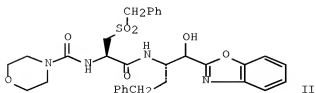
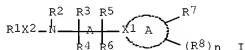
ACCESSION NUMBER: 2000:666718 CAPLUS Full-text

DOCUMENT NUMBER: 133:252041

TITLE: Preparation of amine derivatives as cathepsin
K and cathepsin S inhibitors and in treating
pathology and/or symptomatology of diseases caused by
cysteine protease activity
INVENTOR(S): Link, John O.; Martelli, Arnold J.;
Martichonok, Valeri; Patterson, John W.; Saunders, Oliver
L.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055144	A1	20000921	WO 2000-US6885	
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 2000037507	A	20001004	AU 2000-37507	
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AU 774664	B2	20040701		
EP 1161422	A1	20011212	EP 2000-916397	
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BR 2000009044	A	20020115	BR 2000-9044	
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TR 200103335	T2	20020422	TR 2001-3335	
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HU 2002000572	A2	20020629	HU 2002-572	
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HU 2002000572	A3	20040728		

JP 2002539201	T	20021119	JP 2000-605574
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EE 200100486	A	20030217	EE 2001-486
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US 6576630	B1	20030610	US 2000-525507
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EP 1516877	A1	20050323	EP 2004-15656
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MX 2001009240	A	20020108	MX 2001-9240
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IN 2001KN00948	A	20050311	IN 2001-KN948
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NO 2001004483	A	20011101	NO 2001-4483
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BG 105969	A	20020531	BG 2001-105969
20011002 <--			
HR 2001000736	A1	20021231	HR 2001-736
20011012 <--			
US 20030232864	A1	20031218	US 2003-354888
20030128 <--			
AU 2004201071	A1	20040408	AU 2004-201071
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PRIORITY APPLN. INFO.:			US 1999-124421P P
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			AU 2000-37507 A3
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			EP 2000-916397 A3
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			US 2000-525507 A1
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			WO 2000-US6885 W
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OTHER SOURCE(S):	MARPAT 133:252041		
GI			



AB Title compds. [I; A = heteromonocyclic ring containing 5-6 member; fused heteropolycyclic ring containing 8-14 member; X1 = C, CH; X2 = bond, NHCH2CO, NHCH2CH2SO2, alkylamino; R1 = alkylaminocarbonyl, alkoxycarbonyl, alkylcarbonyl, alkylsulfonyl; R2 = H, alkyl; R3 = alkyl; R4 = H, alkyl; R3R4 = cycloalkylene, heterocycloalkylene; R5 = H; R6 = H; R5R6 = oxo; R7 = CN, Cl, Br, F, NO2, H; R8 = alkyl, alkylidene, CN, Cl, F, Br, NO2; n = 0, 1, 2, 3], N-oxide derivs., prodrug derivs., protected derivs., individual isomers, mixts. of isomers, and pharmaceutically acceptable salts and compns. with bisphosphonic acids or acid esters as excipients are prepared as cathepsin K and cathepsin S inhibitors. Title compds. are administering to animal in treating diseases which cysteine protease activity contributes to the pathol. and/or symptomatol. The diseases are autoimmune disorder, allergic disorder, allogeneic immune response, excessive elastolysis, cardiovascular disorders, fibril formation, etc. Thus, the title compound II was prepared

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2009 ACS on SIN
 ACCESSION NUMBER: 2000:666701 CAPLUS Full-text
 DOCUMENT NUMBER: 133:252050
 TITLE: Preparation of novel N-cyanomethyl amide compounds and compositions as protease inhibitors to treat osteoporosis
 INVENTOR(S): Bryant, Clifford M.; Palmer, James T.; Rydzewski, Robert M.; Setti, Eduardo L.; Tian, Zong-Qiang;
 Venkatraman, Shankar; Wang, Dan-Xiong
 PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 155 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055126	A2	20000921	WO 2000-US6837	
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WO 2000055126	A3	20010222		
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 CA 2368148 A1 20000921 CA 2000-2368148
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 EP 1161415 A2 20011212 EP 2000-916375
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 HU 2002000347 A2 20020629 HU 2002-347
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 US 6455502 B1 20020924 US 2000-526090
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 AT 299493 T 20050715 AT 2000-916375
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 ES 2245303 T3 20060101 ES 2000-916375
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 TW 290132 B 20071121 TW 2000-89104606
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MX 2001009255	A	20020108	MX 2001-9255	
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NO 2001004484	A	20011026	NO 2001-4484	
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BG 106013	A	20020531	BG 2001-106013	
20011012 <--				
HR 2001000737	A1	20021031	HR 2001-737	
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US 20020086996	A1	20020704	US 2001-17851	
20011214 <--				
US 6593327	B2	20030715		
US 20030096796	A1	20030522	US 2002-205600	
20020724 <--				
US 20030119788	A1	20030626	US 2002-241001	
20020909 <--				
US 20040147745	A1	20040729	US 2004-758893	
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US 20070015755	A1	20070118	US 2006-533582	
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PRIORITY APPLN. INFO.:			US 1999-124420P	P
19990315 <--				
			EP 2000-916343	A3
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			US 2000-526090	A1
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			US 2000-526485	A3
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			WO 2000-US6837	W
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			US 2002-205600	B1
20020724 <--				
			US 2004-758893	B1
20040115				
OTHER SOURCE(S):		MARPAT 133:252050		
AB				
<p>Title compds. [R1R2NCR3R4CN; R1 = R11R7NCR5R9X1, R11R8NCR6R10X2NR7CR5R9CX1; X1, X2 independently = CO, CH2SO2; R5, R6 independently = H, C1-6alkyl; R7, R8 independently = H, C1-6alkyl; R9, R10 independently = (un)substituted-C1-6alkyl; R9-R7 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R10-R8 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R5-R9 = C3-8cycloalkylene, C3-8heterocycloalkylene; R10-R6 = C3-8cycloalkylene, C3-8heterocycloalkylene; R11 = X4X5R18; X4 = CO, COO, SO2; X5 = bond, O, NH; R18 = C1-6alkyl; R2 = H, C1-6alkyl; R3 = H, C1-6alkyl; R4 = CN, COOH, COOC1-6alkyl; R2-R4 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R4-R3 = C3-8cycloalkylene, C3-8heterocycloalkylene], N-oxide, prodrug, isomers, pharmaceutically acceptable salts, and composition are prepared as therapeutically effective estrogen receptor agonist.</p> <p>Title compds. are claimed in treating osteoporosis in post-menopausal woman in which cathepsin K activity contributes to the pathol. and symptomatol. of the disease. Thus, the title compound (S)-C6H5CH2OCONHCH(CH2CH(CH3)2)CONHCH2CN was prepared</p>				
REFERENCE COUNT:	13	THERE ARE 13 CITED REFERENCES AVAILABLE		

FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2000:535110 CAPLUS Full-text
 DOCUMENT NUMBER: 133:150414
 TITLE: Synthesis of oligoketides
 INVENTOR(S): Ashley, Gary; Chan-Kai, Isaac Chu-Wah;
 Burlingame, Mark Alma
 PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
 SOURCE: PCT Int. Appl., 87 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000044717	A2	20000803	WO 2000-US2397	
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WO 2000044717	A3	20010208		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2361040	A1	20000803	CA 2000-2361040	
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EP 1144375	A2	20011017	EP 2000-911673	
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JP 2002535387	T	20021022	JP 2000-595973	
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US 6492562	B1	20021210	US 2000-492733	
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EP 1754700	A2	20070221	EP 2006-120607	
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EP 1754700	A3	20070509		
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US 20030096374	A1	20030522	US 2002-214653	

20020807 <--
 US 20030092140 A1 20030515 US 2002-215964
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 US 7022825 B2 20060404
 PRIORITY APPLN. INFO.: US 1999-117384P P
 19990127 <--
 EP 2000-911673 A3
 20000127 <--
 US 2000-492733 A3
 20000127 <--
 WO 2000-US2397 W

20000127 <--
 OTHER SOURCE(S): CASREACT 133:150414

AB Diketide and triketide thioesters were prepared by The method comprises (a) treating benzoxazolinone derivative of diketide or triketide with salt of thiol anion form N-acyl cysteamine thioester of diketide or triketide; (b) treating 2-oxazolidinone derivative of diketide or triketide with lithium salt of thiol anion in the presence of sufficient Lewis acid (trimethylammonium) form N-acyl cysteamine thioester of diketide or triketide. The resulting thioesters may be used as intermediates in the synthesis of desired polyketides by treating a polyketide synthase (PKS) enzyme complex with diketide or polyketide thioester, and may contain functional groups which ultimately reside in side chains on the resulting polyketide and thus can be used further to manipulate the polyketide so as to form derivs. The polyketides produced may also be tailored by glycosylation, hydroxylation and the like by treating polyketide with tailoring enzymes. The method can be used to synthesize oligoketide thioester on a solid support which comprises (1) reacting an N-acyl-2-imidazolidinone coupled to solid support with an aldehyde or acyl moiety under conditions whereby aldehyde or acyl moiety couples to a position α to a carbonyl in the acyl group of the 2-imidazolidinone; (2) optionally repeating step (1); (3) cleaving the resulting oligoketide from solid support by reaction with lithium salt of thiol anion in the presence of Lewis acid providing oligoketide thioester. Or alternately by (1) reacting an N-acyl benzoxazolone coupled to solid support with an aldehyde under conditions whereby aldehyde couples to a position α to carbonyl in the acyl group of the benzoxazolone; (2) optionally repeating step (1); (3) cleaving the resulting oligoketide from the solid support by reaction with salt of thiol anion, providing oligoketide thioester. Thus, propionyl oxazolidinone mixed with anhydrous dichloromethane, flushed with nitrogen, cooled to -15°C in methanol/ice bath; Dibutylboron triflate (in dichloromethane) and diisopropylethylamine were added slowly and resp. to the reaction mixture while keeping temperature below 3°C; After that cooled the temperature to -65°C using dry ice /isopropanol bath, acrolein was added over 5 min by syringe, stirring the reaction mixture for 30 min, after that 1 M aqueous phosphate solution (pH 7.0), methanol, and 2:1 methanol-30% hydrogen peroxide were added resp. as quickly as possible while keeping the temperature below 10°C, the reaction stirred for one more hour, then removed the solvent by rotary evaporation until a slurry remained, further purification giving the desired product (4S)-N-[(2S,3R)-2-methyl-3-hydroxy-4-pentenoyl]-4-benzyl-2-oxazolidinone. 15-Fluoro-6-

deoxyerythronolide B was prepd by feeding (2S,3R)-5-fluoro-3-hydroxy-2-methylpentanoate N-acetyl-cysteamine thioester to S. coelicolor CH999/pJRJ2.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

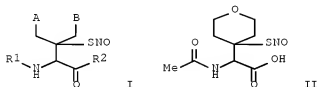
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2000:535107 CAPLUS Full-text
 DOCUMENT NUMBER: 133:150471
 TITLE: Aromatic and heterocyclic S-nitrosothiols
 useful as agents for the treatment of circulatory
 dysfunctions
 INVENTOR(S): Repolles Moliner, Jose; Salas Perez-Rasilla, Eduardo;
 Antonio; Pubill Coy, Francisco; Cerdà Riudavets, Juan
 Lydia; Ferrer Negrie Rofes, Cristina; Cabeza Llorente,
 Banus, Siso, Alicia; Trias Adroher, Nuria; Carbo
 Llaguno, Marcelli; Murat Moreno, Jesus; Michelena
 Pedro
 PATENT ASSIGNEE(S): Lacer, S.A., Spain
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Spanish
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044714	A1	20000803	WO 2000-ES19	
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CA 2359027	A1	20000803	CA 2000-2359027	

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	BR 2000007395	A	20011030	BR 2000-7395
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20000119 <--	GB 2363604	B	20030910	
	DE 10083902	T0	20020110	DE 2000-10083902
20000119 <--	HU 2001005203	A2	20020629	HU 2001-5203
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	JP 2002535385	T	20021022	JP 2000-595971
20000119 <--	JP 3795330	B2	20060712	
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20000119 <--	AU 764725	B2	20030828	AU 2000-30460
20000119 <--	AT 249428	T	20030915	AT 2000-900518
20000119 <--	PT 1157987	T	20040130	PT 2000-900518
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20000119 <--	AP 1439	A	20050630	AP 2001-2247
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BG 105824 A 20020628 BG 2001-105824
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 BG 64983 B1 20061130
 PRIORITY APPLN. INFO.: ES 1999-159 A
 19990127 <-- WO 2000-ES19 W
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 OTHER SOURCE(S): MARPAT 133:150471
 GI



AB The invention relates to novel S-nitrosothiols derived from penicillamine or glutathione, of general formula I [wherein A, B = Ph; or AB = CH₂-Q-CH₂ where Q = O, S, or N-R₃; R₃ = H or C₁-C₄ alkyl; R₁ = C₁-C₅ aliphatic acyl or glutamic acid bonded by γ-carboxy group; R₂ = OH or glycine radical bonded by peptidic linkage so that R₂ = OH when R₁ = aliphatic acyl, and R₂ = glycine when R₁ = glutamic acid]. The compds. exhibit vasodilating and blood platelet aggregation-inhibiting activity, and are useful in the treatment of circulatory system dysfunctions, especially cardiovascular dysfunctions. For instance, 2-amino-2-(4-mercaptotetrahydropyran-4-yl)acetic acid HCl salt was neutralized with NaOH and then N-acetylated with AcCl in MeCN, and the N-acetyl derivative was S-nitrosylated with HCl and NaNO₂ in aqueous MeOH under sonication, to give invention compound II. In an in vitro assay for vasodilation of norepinephrine-contracted arterial rings, II had an EC₅₀ of 0.375 μM, vs. 1.56 μM for the known comparison compound S-nitrosoglutathione, and 0.024-1.89 μM for other invention compds. I.

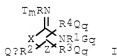
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L9 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2000:493535 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 133:120323
 TITLE: Preparation of 2-aryliminothiazolidines and related compounds progesterone receptor binding agents
 INVENTOR(S): Dixon, Brian R.; Bagi, Cedo M.; Brennan, Catherine R.;
 Brittelli, David R.; Bullock, William H.;
 Chen, Jinshan; Collibee, William L.; Dally, Robert;
 Johnson,

William Jeffrey S.; Kluender, Harold C. E.; Lathrop,
 Aniko M.; F.; Liu, Peiying; Mase, Carol Ann; Redman,
 John J. Scott, William J.; Urbahns, Klaus; Wolanin,
 PATENT ASSIGNEE(S): Bayer Corporation, USA
 SOURCE: PCT Int. Appl., 274 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042031	A2	20000720	WO 1999-US29601	
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WO 2000042031	A3	20001109		
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CA 2359562	A1	20000720	CA 1999-2359562	
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EP 1144396	A2	20011017	EP 1999-968883	
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TR 200102041	T2	20011221	TR 2001-2041	
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HU 2001005134	A2	20020429	HU 2001-5134	
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JP 2002534517	T	20021015	JP 2000-593599	
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MX 2001006675	A	20011203	MX 2001-6675	
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NO 2001003318	A	20010830	NO 2001-3318	
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IN 2001MN00824	A	20050304	IN 2001-MN824	
20010713 <--				

BG 105761 A 20020329 BG 2001-105761
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 PRIORITY APPLN. INFO.: US 1999-231906 A
 19990114 <-- WO 1999-US29601 W
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 OTHER SOURCE(S): MARPAT 133:120323
 GI



AB Title compds. (I; T = alkyl, alkoxy, aryl, CO₂H, alkenyl, alkynyl, CHO, OH, NO₂, cyano, halo, OCF₃, etc.; R = aryl, heteroaryl; R₁ = alkyl, cycloalkyl, heterocycloalkyl, alkenyl, cycloalkenyl, alkynyl; R₂-R₄ = H, alkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, halo, O, etc.; X = O, S, SO, SO₂; G = halo, OH, O, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, aryl, heteroaryl, etc.; m = 1-5; p, q = 0-4; Z = CnH_{2n-r}; n = 2-5; r = sum of non-H substituents R₂, R₃, R₄; with provisos), were prepared. Thus, title compound (II), prepared from 2-chloroethylammonium chloride, 2-methyl-4-nitrophenyl isothiocyanate, and iso-Bu bromide, at 200 nM gave 80-100% inhibition of 3H-progesterone to the progesterone receptor.

L9 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2000:421131 CAPLUS Full-text
 DOCUMENT NUMBER: 133:43432
 TITLE: Preparation of
 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindoles
 as
 inhibitors of cyclin-dependent kinases, in
 particular
 CDK2
 INVENTOR(S): Chen, Yi; Corbett, Wendy Lea; Dermatakis,
 Apostolos;
 Liu, Jin-jun; Luk, Kin-chun; Mahaney, Paige
 E.,
 Mischke, Steven Gregory
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
 SOURCE: PCT Int. Appl., 170 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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MD, MG,      MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL,      TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW
      RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
CY, DE,      DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,
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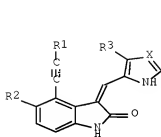
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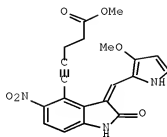
OTHER SOURCE(S):

MARPAT 133:43432

GI



I



II

AB The title compds. (I) [wherein R1 = H, acyl, carboxy, carbamido, (un)substituted (cyclo)alkyl, or heterocyclcyl; R2 = H, alkoxy, acyl(oxy), carboxy, carbamido, halogen, NO2, CN, sulfamido, perfluoroalkyl, alkyl, etc.; R3 = H, alkoxy, acyl(oxy), carboxy, carbamido, halogen, CN, amino, perfluoroalkyl, alkyl, etc.; X = N or (un)substituted C] and their intermediates and analogs were prepared by reaction of alkynes with 4-halo-2-oxoindoles. I inhibit cyclin-dependent kinases (CDKs), especially CDK2, and are useful as anti-proliferative agents in the treatment or control of cell proliferative disorders, in particular breast and colon tumors. For example, Me 4-pentynoate was coupled with (Z)-4-bromo-1,3-dihydro-3-[(3-methoxy-1H-pyrrol-2-yl)methylene]-5-nitro-2H-indole-2-one (preparation given) using (Ph3P)2PdCl2 and CuI as catalysts in DMF and TEA to give (Z)-II in 72% yield. In a CDK2 flash plate assay, II inhibited CDK2 by > 90% at concns. of $\leq 1.0 \mu\text{M}$. Representative compds. of the invention were tested in cell-based assays against epithelial breast carcinoma line MDA-MB435 and colon carcinoma line SW480 and gave IC50 values of < 3.5 μM and < 1.0 μM , resp. Formulations for tablets, capsules, and injection solution/emulsion preps. are also included.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L9 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1954:11089 CAPLUS Full-text

DOCUMENT NUMBER: 48:11089

ORIGINAL REFERENCE NO.: 48:2058c-i, 2059a-h

TITLE: Some reactions of 2-alkoxy -3,4-dihydro-2H-pyrans

AUTHOR(S): Longley, Raymond I., Jr.; Emerson, Wm. S.; Shafer,

Theodore C.

CORPORATE SOURCE: Monsanto Chem. Co., Dayton, O.

SOURCE: Journal of the American Chemical Society (1952
, 74, 2012-15
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 48:11089

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

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Make the stem longer and try again. For example, if your original
term was 'degr?' to search for variations and the abbreviation for
'degradation', you could replace it with the expression '(degrdn OR
degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the
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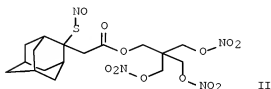
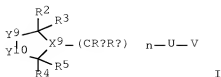
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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:836762 CAPLUS Full-text
DOCUMENT NUMBER: 139:350474
TITLE: Preparation and compositions of nitrosothio
(hetero)cyclic nitric oxide donors
INVENTOR(S): Fang, Xinqin; Garvey, David S.; Gaston, Ricky
D.; Lin,
Chia-en; Ranatunga, Ramani R.; Richardson,
Stewart K.;
Wang, Tiansheng; Wang, Weiheng; Wey, Shioh-jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 2003086282	A2	20031023	WO 2003-US10562	

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 WO 2003086282 A3 20040429
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 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
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 US 20030203915 A1 20031030 US 2003-407420
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 JP 2005537223 T 20051208 JP 2003-583309
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 PRIORITY APPLN. INFO.: US 2002-369873P P
 20020405 <--
 WO 2003-US10562 W
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 OTHER SOURCE(S): MARPAT 139:350474
 GI



AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO2; X9 = CR10 or N; Y9 = CR6R7, NRi, NR25, NRiCR6R7, CR6R7NRi, CR2R3CR6R7, or CR6R7CR2R3; Y10 = CR8R9 or CR8R9CR17R18; R2-R9, R17, and R18 = independently H or alkyl; or R2R3, R4R5, R6R7, or R8R9 = independently oxo; or R4 and R7 together with the C's to which they are attached = cycloalkyl; or CR6R7 = cycloalkyl; R6 and R9 taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R7 and R8 are not present; R4 and R25 taken together with the C and N to which they are attached = heterocyclyl; Ra = lone pair of electrons, H, or (aryl)alkyl; Re and Rf = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CR6Rf = heterocyclyl or (bridged) cycloalkyl; Ri = H or (un)substituted alkyl, aryl, carboxamido, sulfonamido, etc.; n = 0-3; and pharmaceutically acceptable salts thereof] were prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiolo. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH2Cl2 to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC50 of 5 μM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight inhibition, or exhibited much higher IC50 values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting

wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:51274 CAPLUS Full-text
 DOCUMENT NUMBER: 136:96100
 TITLE: Use of dammarane-type triterpenoid saponins
 INVENTOR(S): Raj Kumar, Chinni Krishnan
 PATENT ASSIGNEE(S): Raj Kumar, Sujatha, India; Argaet, Victor Peter
 SOURCE: PCT Int. Appl., 125 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003996	A1	20020117	WO 2001-AU837	
20010712 <--				
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OTHER SOURCE(S): MARPAT 136:96100				

AB The present invention discloses the use of a dammarane-type triterpenoid saponin or derivative or pharmaceutically acceptable salt thereof for treating or preventing conditions, which are related to reduced nitric oxide levels, or which are ameliorable or preventable by augmentation of nitric oxide levels, within the human body, or for promoting responses requiring enhanced nitric oxide levels within the human body. A saponin extract obtained from *Bacopa monnieri* is shown to induce vascular nitric oxide production in rabbit aorta rings, to enhance growth of human neuroblastoma cells (neuronal filament formation), to reduce expression of amyloid precursor protein in HeLa cells transfected with the APP, to prevent leg cramps and decrease involuntary muscle movements in a patient, to cure chilblains in another patient, and to enhance the quantity and quality (protein and vitamin level) of milk in Jersey cows.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS

RE FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:790495 CAPLUS Full-text

DOCUMENT NUMBER: 133:350092

TITLE: Thromboxane ligands without blood clotting side

effects

INVENTOR(S): Burk, Robert M.; Krauss, Achim H.; Woodward, David F.

PATENT ASSIGNEE(S): Allergan Sales, Inc., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

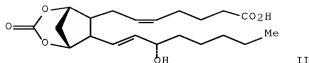
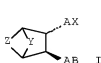
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PRIORITY APPLN. INFO.:		US 1999-301794		A

19990429 <--

OTHER SOURCE(S):

MARPAT 133:350092

GI



AB A method of treating ocular hypotension, hypertension, hemorrhage, myocardial ischemia, angina pectoris, coronary contraction, cerebrovascular contraction after subarachnoidal hemorrhage, cerebral hemorrhage and asthma which comprises administering to a mammal suffering therefrom a therapeutically effective amount of a thromboxane ligand which is a compound of formula I [Y = (CH₂)_n; Z = O, OCH₂, O-CO-O, (CR₂)_n; n = 1-2; R = alkyl; A = (substituted) alkylene or alkenylene; B = Me, cycloalkyl, aryl, etc.; X = nitro, cyano, CO₂H, CH₂OH, CONH₂, etc.]. Pharmaceutical comps. containing I are described. Thus, II was prepared from PGF₂α, and showed a decrease in dog intraocular pressure at a dose of 0.01%.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

=> s 12 and (5HT?)

6995 L2

9202 5HT?

L5 31 L2 AND (5HT?)

=> s 15 and (py<2003 or ay<2003 or pry<2003)

22983475 PY<2003

4504208 AY<2003

3973137 PRY<2003

L6 5 L5 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d 16 ibib abs 1-5

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:451629 CAPLUS Full-text

DOCUMENT NUMBER: 141:23543

TITLE: Preparation of N-substituted piperidine derivatives as

serotonin receptor agents

INVENTOR(S): Andersson, Carl-Magnus; Schlienger, Nathalie; Fejzic,

Alma; Hansen, Eva Louise; Pawlas, Jan

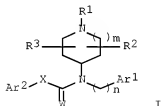
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., Swed.

SOURCE: U.S. Pat. Appl. Publ., 44 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040106600	A1	20040603	US 2003-601070	
20030620 <--				
US 7253186	B2	20070807		
US 20060094758	A1	20060504	US 2005-299566	
20051212 <--				
US 20060199818	A1	20060907	US 2006-417866	
20060503 <--				
US 7476682	B2	20090113		
US 20060205722	A1	20060914	US 2006-418353	
20060503 <--				
IN 2006KO01272	A	20070706	IN 2006-KO1272	
20061124 <--				
IN 2006KO01273	A	20070706	IN 2006-KO1273	
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AU 2007203444	A1	20070816	AU 2007-203444	
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PRIORITY APPLN. INFO.:			DK 2002-973	A
20020624 <--				
			US 2002-391269P	P
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			AU 2003-247615	A3
20030620				
			US 2003-601070	A1
20030620				
			IN 2004-KN1959	A3
20041220				
			US 2005-299566	A1
20051212				
OTHER SOURCE(S):	MARPAT 141:23543			
GI				



AB Disclosed herein are compds. of formula (I), pharmaceutically acceptable salts, amides, esters, or prodrugs thereof [whwherein R1 = each (un)substituted heterocyclyl or heterocyclyl-C1-6 alkyl; R2, R3 = H, C1-6 alkyl, or halogen or such that R2 together with R3 forms a ring; m = 0, 1, 2; n = 1, 2, 3; Ar1 = each

(un)substituted aryl or heteroaryl; W = O, S; X = each (un)substituted methylene, ethylene, propylene, or vinylene, CH₂NR (wherein R = H, C1-6 alkyl); Ar₂ = each (un)substituted aryl or heteroaryl]. Also disclosed are. (1) methods of inhibiting an activity of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an effective amount of one or more of the compds. of formula I, (2) methods of inhibiting an activation of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an effective amount of one or more of the compds. of formula I, and (3) methods of treating a disease condition associated with a monoamine receptor, in particular serotonin receptor 5-HT_{2A} subclass. The disease condition is selected from (a) the group consisting of schizophrenia, schizoaffective disorders, psychosis, drug induced psychosis, and side effects observed with the treatment of chronic neurodegenerative disorders with a selective serotonin reuptake inhibitor (SSRI), wherein said neurodegenerative disorder is selected from Alzheimer's disease, Parkinson's disease, Lewy body dementia, frontotemporal dementia, spinocerebellar atrophy, and Huntington's disease, and (b) the group consisting of Reynaud's Phenomena, migraine, hypertension, thrombosis, vasospasm, ischemia, depression, anxiety, motor tics, Tourette's syndrome, dyskinesias, on/off phenomena, tremor, rigidity, bradykinesia, psychomotor slowing, addiction, including alc. addiction, opioid addiction, and nicotine addiction, sleep disorders, appetite disorders, and decreases in libido and ejaculatory problems. Thus, N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)-N-[1-[3-(4-(S)-isopropyl-2-oxoxazolidin-3-yl)propyl]piperidin-4-yl]acetamide oxalate, which was prepared by alkylation of N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)-N-piperidin-4-ylacetamide with (4S)-3-(3-chloropropyl)-4-isopropylloxazolidin-2-one, inhibited 5-HT_{2A} receptor by 104% in a receptor selection and amplification (R-SAT) assay using NIH3T3 cells.

REFERENCE COUNT: 255 THERE ARE 255 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:267331 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:303669

TITLE: Preparation of N-(piperidin-4-ylmethyl)imidazopyridinecarboxamides as 5-HT₄ receptor modulators

INVENTOR(S): Katsu, Yasuhiro; Kon-I, Kana; Morita, Mikio; Noguchi,

Hirohide; Uchida, Chikara
PATENT ASSIGNEE(S): Pfizer Pharmaceuticals Inc., Japan; Pfizer Inc.

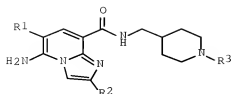
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004026868	A1	20040401	WO 2003-IB3945	
20030908 <--				
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499494	A1	20040401	CA 2003-2499494	
20030908 <--				
AU 2003259482	A1	20040408	AU 2003-259482	
20030908 <--				
EP 1543004	A1	20050622	EP 2003-797450	
20030908 <--				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014584	A	20050809	BR 2003-14584	
20030908 <--				
JP 2006502180	T	20060119	JP 2004-537407	
20030908 <--				
US 20040127514	A1	20040701	US 2003-667182	
20030917 <--				
US 6951867	B2	20051004		
MX 2005003065	A	20050527	MX 2005-3065	
20050318 <--				
PRIORITY APPLN. INFO.:			US 2002-412426P	P
20020920 <--				
			WO 2003-IB3945	W
20030908				
OTHER SOURCE(S):	MARPAT 140:303669			
GI				



I

AB The title compds. [I; R1 = H, halo; R2 = H, alkyl, aminocarbonyl, mono- or dialkylaminocarbonyl; R3 = alkyl which is substituted by at least one substituent selected from the group consisting of substituents α ; said substituents α = aryl, OH, oxo, heterocyclyl, etc.] which have 5-HT₄ receptor binding activity, and thus are useful for the treatment of gastroesophageal reflux disease, non-ulcer dyspepsia, functional dyspepsia, irritable bowel syndrome or the like in mammalian, especially humans, were prepared E.g., a multi-step synthesis of I [R1 = Cl; R2 = H; R3 = 3,3-dimethyl-2-oxobutyl], starting from Et 6-[(2,2,-dimethylpropanoyl)amino]-2-fluoronicotinate, was given. All compds. I prepared in the working examples showed K_i of 0.19 nM to 47 nM with respect to the affinity to the 5-HT₄ receptor. This invention also provides a pharmaceutical composition comprising the compound I.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:2854 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:77030

TITLE: Preparation of 1,4-disubstituted piperidines as

serotonin 5-HT_{2A} inverse agonists.

INVENTOR(S): Andersson, Carl-Magnus; Schlienger, Nathalie; Fejzic,

Alma; Hansen, Eva Louise; Pawlas, Jan

PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

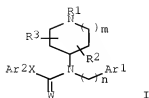
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000808	A2	20031231	WO 2003-US19797	
20030620 <--				
WO 2004000808	A3	20040325		
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	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,			

GE, GH,
 LK, LR,
 NZ, OM,
 TN, TR,
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY,
 EE, ES,
 SK, TR,
 TD, TG
 CA 2490397 A1 20031231 CA 2003-2490397
 20030620 <--
 AU 2003247615 A1 20040106 AU 2003-247615
 20030620 <--
 AU 2003247615 B2 20070809
 BR 2003012217 A 20050510 BR 2003-12217
 20030620 <--
 EP 1562937 A2 20050817 EP 2003-761275
 20030620 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1675201 A 20050928 CN 2003-818839
 20030620 <--
 JP 2005533813 T 20051110 JP 2004-516166
 20030620 <--
 NZ 537522 A 20060728 NZ 2003-537522
 20030620 <--
 RU 2320646 C2 20080327 RU 2005-101414
 20030620 <--
 MX 2004012893 A 20050331 MX 2004-12893
 20041217 <--
 IN 2004KN01959 A 20051021 IN 2004-KN1959
 20041220 <--
 ZA 2004010408 A 20050922 ZA 2004-10408
 20041223 <--
 IN 2006KO01272 A 20070706 IN 2006-KO1272
 20061124 <--
 IN 2006KO01273 A 20070706 IN 2006-KO1273
 20061124 <--
 AU 2007203444 A1 20070816 AU 2007-203444
 20070724
 PRIORITY APPLN. INFO.: US 2002-391269P P
 20020624 <--
 AU 2003-247615 A3
 20030620
 WO 2003-US19797 W
 20030620
 IN 2004-KN1959 A3
 20041220
 OTHER SOURCE(S): MARPAT 140:77030

GI



AB Title compds. [I; R1 = (substituted) heterocyclyl, heterocyclylalkyl; R2, R3 = H, alkyl, halo; R2R3 = atoms to form a ring; m = 0-2; n = 1-3; Ar1 = (substituted) aryl, heteroaryl; W = O, S; X = (substituted) methylene, ethylene, propylene, vinylene, CH2N(Rn); Rn = H, alkyl; Ar2 = (substituted) aryl, heteroaryl], were prepared. Thus, a mixture of N-(4-fluorobenzyl)-N-(piperidin-4-yl)-2-(4-isobutoxyphenyl)acetamide, K2CO3, NaI, and (4S)-3-(3-chloropropyl)-4-isopropylloxazolidinon-2-one were stirred overnight to give 71% N-(4-fluorobenzyl)-2-(4-isobutoxyphenyl)-N-[1-[3-(4-(S)-isopropyl-2-oxooxazolidin-3-yl)propyl]piperidin-4-yl]acetamide oxalate (117NLS01). The latter showed pIC50 = 9.7 for repression of 5-HT2A receptor activity.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:991179 CAPLUS [Full-text](#)
 DOCUMENT NUMBER: 140:27759
 TITLE: Preparation of
 spiro[9,10-dihydroanthracene]-9,3'-pyrrolidine
 (SPAN) and its derivatives as selective serotonin

receptor antagonists

INVENTOR(S): Glennon, Richard; Westkaemper, Richard
 PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
 SOURCE: U.S. Pat. Appl. Publ., 21 pp., which
 CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030232872	A1	20031218	US 2003-429970	

20030506 <--

US 6806283
PRIORITY APPLN. INFO.:
20020506 <--

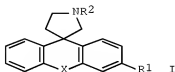
B2 20041019

US 2002-377606P P
US 2003-438798P P

20030109

OTHER SOURCE(S):
GI

MARPAT 140:27759



AB The title compds. [I; R1, R2 = H, OH, OMe, halo, aryl, etc.; X = (un)substituted CH2; O, S, SO2] which are selective, high affinity antagonists of 5-HT2 serotonin receptors useful as antidepressant and antianxiety agents, were prepared E.g., a multi-step synthesis of SPAN [I; R1, R2 = H; X = CH2] (starting from 9,10-dihydroanthracenecarboxamide) which showed Ki of 3.8 nM against 5-HT2A receptor binding, was given. Several compds. I also displayed a high affinity for the histamine H1 receptor. Thus, SPAN showed Ki of 8.5 nM against H1 receptor binding. Pharmaceutical composition comprising the compound I is claimed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:152309 CAPLUS Full-text

DOCUMENT NUMBER: 134:193415

TITLE: Preparation of heteroannulated pyridines as 5-HT1A

receptor ligands

INVENTOR(S): Peglioni, Jean-louis; Dessinges, Aimee; Poitevin,

Christophe; Millan, Mark; Dekeyne, Anne
PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.; Les Laboratoires

Servier

SOURCE: Eur. Pat. Appl., 27 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 1078928	A1	20010228	EP 2000-402359	
20000825 <--				

EP 1078928 B1 20040512
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT, IE, SI, LT, LV, FI, RO
 FR 2797874 A1 20010302 FR 1999-10834
 19990827 <--
 FR 2797874 B1 20020329
 US 6399616 B1 20020604 US 2000-641777
 20000818 <--
 JP 2001097978 A 20010410 JP 2000-252191
 20000823 <--
 JP 3602780 B2 20041215
 MX 2000008241 A 20020820 MX 2000-8241
 20000823 <--
 CA 2317053 A1 20010227 CA 2000-2317053
 20000825 <--
 ZA 2000004411 A 20010228 ZA 2000-4411
 20000825 <--
 CN 1286255 A 20010307 CN 2000-124065
 20000825 <--
 CN 1163495 C 20040825
 HU 2000003413 A2 20010730 HU 2000-3413
 20000825 <--
 HU 2000003413 A3 20031128
 AT 266664 T 20040515 AT 2000-402359
 20000825 <--
 PT 1078928 T 20040930 PT 2000-402359
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 ES 2220359 T3 20041216 ES 2000-402359
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 NO 2000004295 A 20010228 NO 2000-4295
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 NO 316651 B1 20040322
 BR 2000003848 A 20010403 BR 2000-3848
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 AU 765661 B2 20030925 AU 2000-53642
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 HK 1034250 A1 20050429 HK 2001-104815
 20010711 <--
 US 20020161228 A1 20021031 US 2002-105171
 20020325 <--
 US 6486171 B2 20021126
 PRIORITY APPLN. INFO.: FR 1999-10834 A
 19990827 <-- US 2000-641777 A3
 20000818 <--
 OTHER SOURCE(S): MARPAT 134:193415
 GI



AB Title compds. [I; R1 = R(CH2)nZZ1; R = (un)substituted naphthyl or heteroannelated Ph; R2R3 = atoms to complete a thiophene, furan, or (oxo)pyrrole ring; Z = bonds, O, [(ar)alkyl]imino; Z1 = 1,4-cyclohexylene, piperidine-1,4- or -4,1-diyl, piperazine-1,4-diyl; n = 1-6] were prepared Thus, 7-chlorofuro[2,3-c]pyridine was aminated by N-(2-naphthylmethyl)-4-piperidineamine to give I (R1 = RCH2NHZ1, R = 2-naphthyl, R2R3 = OCH:CH, Z1 = piperidine-4,1-diyl). Data for biol. activity of I were given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l2 and (NE?)

6995 L2
7712571 NE?

L7 2935 L2 AND (NE?)

=> s l2 and (NE?) and (constric? or dilat? or flush? or sweat? or flash?)

6995 L2
7712571 NE?
27608 CONSTRIC?
63379 DILAT?
26045 FLUSH?
10530 SWEAT?
76912 FLASH?

L8 47 L2 AND (NE?) AND (CONSTRIC? OR DILAT? OR FLUSH? OR SWEAT? OR

FLASH?)

=> s l8 and (py<2003 or pry<2003 or ay<2003)

22983475 PY<2003
3973137 PRY<2003
4504208 AY<2003

L9 12 L8 AND (PY<2003 OR PRY<2003 OR AY<2003)

=> d 19 ibib abs 1-5

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1028086 CAPLUS Full-text

DOCUMENT NUMBER: 143:326396

TITLE: Preparation of piperidinyl- and piperazinyl-sulfonylmethyl hydroxamic acids

and their

use as protease inhibitors

INVENTOR(S): Mcdonald, Joseph J.; Kassab, Darren J.; Massa, Mark

A.; Grapperhaus, Margaret L.; Schmidt,

Michelle A.;

Rico, Joseph G.; Mullins, Patrick B.; Brown,

David L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 417 pp., Cont.-in-part

of U.S.

Ser. No. 618,288.

CODEN: USXXCO

Patent

English

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT: 3

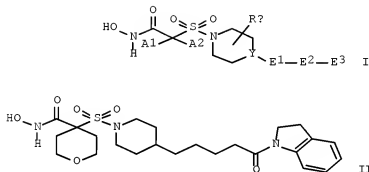
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050209278	A1	20050922	US 2003-700202	
20031103 <--				
US 20050009838	A1	20050113	US 2003-618288	
20030425 <--				
US 7119203	B2	20061010		
CA 2543715	A1	20050512	CA 2004-2543715	
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WO 2005042521	A2	20050512	WO 2004-US36666	
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WO 2005042521	A3	20050707		
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CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				
GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,				
KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				
NA, NI,				
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				
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NE, SN, TD, TG				
EP 1689743	A2	20060816	EP 2004-810297	
20041103				
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BR 2004015885	A	20070102	BR 2004-15885	
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JP 2007510732	T	20070426	JP 2006-539634	
20041103				
MX 2006004944	A	20060804	MX 2006-4944	
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PRIORITY APPLN. INFO.:			US 2002-375598P	P
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			US 2002-380713P	P
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20020627 <--	US 2002-392021P	P
20030425	US 2003-618288	A2
20031103	US 2003-700202	A
20041103	WO 2004-US36666	W

OTHER SOURCE(S): CASREACT 143:326396; MARPAT 143:326396
GI

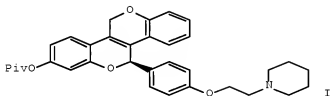


AB Title compds. I [A1 and A2 together with the C to which they are bonded join to form (un)substituted heterocyclyl or carbocyclyl, or A1 and A2 are independently selected from H, alkyl, alkoxyalkyl, alkenyl, alkynyl, etc.; Rx = H, halo, CN, OH, NO₂, alkyl, alkenyl, alkoxy, alkoxyalkyl, heterocyclyl, etc.; Y = N, CH, or CR_x; E1 = (un)substituted carbocyclyl, heterocyclyl, etc.; E2 = O, CO, C(O)O, OC(O), bond, S, etc.; E3 = halo, CN, (un)substituted alkyl, alkenyl, alkynyl, heterocyclyl, heterocyclylalkyl, etc.] and their pharmaceutically acceptable salts are prepared and disclosed as protease inhibitors. E.g., a multi-step synthesis of II, starting from Et crotyl phosphonate and tert-Bu 4-[(4-formylpiperidin-1-yl)sulfonyl]tetrahydro-2H-pyran-2H-pyran-4- carboxylate, was given. This invention is directed generally to proteinase (also known as 'protease') inhibitors, and more particularly, inhibitors of matrix metalloproteinase (also known as 'matrix metalloprotease' or 'MMP'), aggrecanase, or TNF- α convertase activity. In assays to determine inhibition consts. (K_i) against MMP-1, MMP-2, MMP-9, MMP-13 and MMP-14, I possessed values ranging from 0.13->10,000. This invention also is directed to compns. of such hydroxamic acids, intermediates for the syntheses of such hydroxamic acids, methods for making such hydroxamic acids, and methods for treating conditions (particularly pathol. conditions) associated with MMP, aggrecanase, or TNF- α convertase activity.

ACCESSION NUMBER: 2004:1127099 CAPLUS Full-text
 DOCUMENT NUMBER: 142:56279
 TITLE: Preparation of tetracyclic heterocycles as
 selective
 estrogen receptor modulators (SERMs).
 INVENTOR(S): Kanojia, Ramesh M.; Jain, Nareshkumar F.; Ng,
 Raymond;
 Sui, Zhihua; Xu, Jiayi
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 110 pp., Cont.-in-part
 of U.S. Ser. No. 307,735.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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20031121 <--	US 20040259915	A1	20041223	US 2003-719875	
	US 7105679	B2	20060912		
	US 20030216463	A1	20031120	US 2002-307735	
20021202 <--	US 7329654	B2	20080212		
	CA 2505857	A1	20040617	CA 2003-2505857	
20031121 <--	WO 2004050660	A1	20040617	WO 2003-US37419	
20031121 <--	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,				
CH, CN,	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,				
GE, GH,	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
LK, LR,	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,				
NZ, OM,	PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN,				
TR, TT,	TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				
AZ, BY,	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				
EE, ES,	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK,				
TR, BF,	BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003295822	A1	20040623	AU 2003-295822	
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20031121 <--	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,				
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	BR 2003016843	A	20051101	BR 2003-16843	

20031121 <--	CN 1745085	A	20060308	CN 2003-80109395	
20031121 <--	JP 2006514941	T	20060518	JP 2004-557261	
20031121 <--	NZ 539914	A	20080328	NZ 2003-539914	
20031121 <--	RU 2331645	C2	20080820	RU 2005-116845	
20031121 <--	MX 2005005897	A	20060208	MX 2005-5897	
20050602 <--	IN 2005KN01262	A	20070720	IN 2005-KN1262	
20050629 <--	ZA 2005005324	A	20060927	ZA 2005-5324	
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20011219 <--				US 2002-307735	A2
20021202 <--				WO 2003-US37419	W
20031121					
OTHER SOURCE(S):	CASREACT 142:56279				
GI					



AB There are 5 claimed compds., e.g., I and over 100 synthetic examples of selective estrogen receptor modulators. Thus, 3-(2-hydroxy-4-methoxyphenyl)-7-hydroxy-4-methylchromen-2-one (preparation given), in methanol/acetone was added at room temperature anhydrous potassium carbonate; the solution was stirred 2 h to give 2,8-dihydroxy-1H-chromeno[4,3-c]chromen-5-one. The latter bound to estrogen α and β receptors at 0.505 μ M and 0.061 μ M, resp. I are useful in the treatment and/or prevention of disorders associated with the depletion of estrogen such as hot flashes, vaginal dryness, osteopenia and osteoporosis; hormone sensitive cancers and hyperplasia of the breast, endometrium, cervix and prostate; endometriosis, uterine fibroids, osteoarthritis and as contraceptive agents, alone or in combination with a progestogen or progestogen antagonist.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS

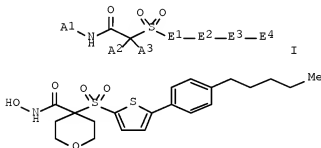
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2004:467885 CAPLUS Full-text
 DOCUMENT NUMBER: 141:38527
 TITLE: Preparation of heteroarylsulfonylmethyl
 hydroxamic acids and amides and their use as protease
 inhibitors
 INVENTOR(S): Becker, Daniel P.; Carroll, Jeffery N.;
 Fobian, Yvette M.; Grapperhaus, Margaret L.; Hansen, Donald
 W., Jr.; Heintz, Robert M.; Kassab, Darren J.; Massa,
 Mark A.; McDonald, Joseph J.; Nagy, Mark A.; Pitzele,
 Barnett S.; Rico, Joseph G.; Schmidt, Michelle A.;
 Spangler, Dale P.
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 252 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004048368	A2	20040610	WO 2003-US37942	
20031124 <--				
WO 2004048368	A3	20040812		
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AU 2003300800	A1	20040618	AU 2003-300800	
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EP 1565459	A2	20050824	EP 2003-812052	
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003016506	A	20051004	BR 2003-16506	
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JP 2006513270	T	20060420	JP 2005-510336	
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US 20040142979	A1	20040722	US 2003-722104	
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PRIORITY APPLN. INFO.:			US 2002-429068P	P
20021125 <--				
			US 2003-504281P	P
20030919			WO 2003-US37942	W
20031124				
OTHER SOURCE(S):	MARPAT 141:38527			
GI				



AB Title compds. I [wherein A1 = H, OH, cycloalkyloxy, heterocycloxy; A2, A3 = independently H, (un)substituted (cyclo)alkyl(thio), alkanyl, alkynyl, heterocyclyl, etc.; or CA2A3 = (un)substituted cycloalkyl, heterocyclyl, such as tetrahydropyranyl; E1 = (un)substituted heteroaryl; E2 = (un)substituted cycloalkyl; E3 = a bond, O, CO, CO2, OCO, S, SO, SO2, OSO2, SO2O, C(=NH), C(=NOH), (un)substituted NH, CONH, NHCO, CONHNHCO, NHCONH, NHSO2, SO2NH, NHC(=NH), NHC(=NOH), C(=NH)NH, C(=NOH)NH, (carbonyl)alkyl, alkanyl, alkanoyl; E4 = H, halo, CN, (un)substituted (cyclo)alkyl, alkanyl, alkynyl, heterocyclyl; and salts thereof] were prepared as inhibitors of protease activity, particularly matrix metalloproteinase (MMP), TNF- α convertase, or aggrecanase activity. For example, coupling of 2-thiopheneboronic acid with 4-butoxybromobenzene gave 2-(4-butoxyphenyl)thiophene (588), which was treated with Me disulfide and Oxone to afford the 5-(methylsulfonyl)thiophene derivative (588). Reaction of the Me sulfone with t-Bu carboxylate anhydride using lithium bis(trimethylsilyl)amide provide the tert-Bu α -(thienylsulfonyl)acetate (898). Tert-Bu 4-[[5-(4-butoxyphenyl)thien-2-yl]sulfonyl]tetrahydro-2H-pyran-4-carboxylate (911) was produced by cycloaddn. of the acetate with bis(bromoethyl) ether in the presence of 18-crown-6.

Deesterification (85%) with TFA, followed by amidation (100%) with O-(tetrahydro-2H-pyran-2-yl)hydroxylamine and O-deprotection (74%) with HCl gave II. The latter inhibited the human recombinant MMP-1, MMP-2, MMP-9, MMP-13, and MMP-14 cleavage of peptide substrates with Ki values of >1250 nM, 0.483 nM, 0.806 nM, 0.127 nM, and 466 nM, resp. Thus, I and their pharmaceutical comps. are useful for treating tissue destruction, fibrotic diseases, matrix weakening, defective injury repair, cardiovascular disease, pulmonary disease, kidney disease, liver disease, ophthalmol. disease, and/or CNS diseases (no data).

L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:875282 CAPLUS Full-text
 DOCUMENT NUMBER: 139:364961
 TITLE: Preparation of piperidinyl- and
 piperazinyl-sulfonylmethyl hydroxamic acids
 and their
 use as protease inhibitors
 INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell,
 Louis J.;
 Boehm, Terri L.; Brown, David L.; Carroll,
 Jeffery N.;
 Chen, Yiyuan; Fobian, Yvette; Freskos, John
 N.;
 Gasiecki, Alan F.; Grapperhaus, Margaret;
 Heintz,
 Robert M.; Hockerman, Susan L.; Kassab, Darren
 J.;
 Khanna, Ish Kumar; Kolodziej, Stephen A.;
 Massa, Mark;
 Mcdonald, Joseph; Mischke, Brent V.; Mischke,
 Deborah
 A.; Mullins, Patrick B.; Nagy, Mark; Norton,
 Monica
 B.; Rico, Joseph G.; Schmidt, Michelle A.;
 Stehle,
 Nathan W.; Talley, John J.; Vernier, William
 F.;
 Villamill, Clara I.; Wang, Lijuan Jane; Wynn,
 Thomas
 A.
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA; et al.
 SOURCE: PCT Int. Appl., 819 pp.
 CODEN: P1XXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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----	WO 2003091247	A2	20031106	WO 2003-US13123	
20030425 <--					
	WO 2003091247	A3	20040115		
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 CA 2483314 A1 20031106 CA 2003-2483314
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 AU 2003221786 A1 20031110 AU 2003-221786
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 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 BR 2003009671 A 20050503 BR 2003-9671
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 JP 2005537228 T 20051208 JP 2003-587805
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 MX 2004010555 A 20050217 MX 2004-10555
 20041022 <--
 PRIORITY APPLN. INFO.: US 2002-375598P P
 20020425 <--
 US 2002-380713P P
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 US 2002-392021P P
 20020627 <--
 WO 2003-US13123 W
 20030425
 OTHER SOURCE(S): MARPAT 139:364961
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
 PRINT *

AB Title compds. I [A1 and A2 together with the C to which they are
 bonded join to form (un)substituted-heterocyclyl or -carbocyclyl,
 or A1 and A2 are independently selected from H, alkyl,
 alkoxyalkyl, alkenyl, alkynyl, etc.; Rx = H, halo, CN, OH, NO2,
 alkyl, alkenyl, alkoxy, alkoxyalkyl, heterocyclyl, etc.; Y = N,
 CH, or CRx; E1 = (un)substituted heteroaryl; E2 = O, CO, C(O)O,
 OC(O), bond, S, etc.; E3 = halo, CN, (un)substituted-alkyl, -

alkenyl, -alkynyl, -heterocyclyl, heterocyclylalkyl, etc.] and their pharmaceutically acceptable salts are prepared and disclosed as protease inhibitors. Thus, e.g., II·HCl was prepared with piperazine ring formation occurring via cyclization of 2,2,2-trifluoroethoxyaniline (preparation given) with N,N-di(2-chloroethyl)methylsulfonamide (preparation given) to provide piperazinyl intermediate III which was converted in five addnl. steps to the desired product. This invention is directed generally to proteinase (also known as 'protease') inhibitors, and more particularly, inhibitors of matrix metalloproteinase (also known as 'matrix metalloprotease' or 'MMP') activity and/or aggrecanase activity. In assays to determine inhibition consts. (Ki) against MMP-1, MMP-2, MMP-9, MMP-13 and MMP-14, I possessed values ranging from 0.13->10,000. This invention also is directed to compns. of such hydroxamic acids, intermediates for the syntheses of such hydroxamic acids, methods for making such hydroxamic acids, and methods for treating conditions (particularly pathol. conditions) associated with MMP activity and/or aggrecanase activity.

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:717760 CAPLUS Full-text

DOCUMENT NUMBER: 139:245903

TITLE: Preparation of
[(hetero)arylsulfonylamino]-[1-substituted-
piperidin-4-

yl]-acetic acids as metalloprotease inhibitors
Pikul, Stanislaw; Ohler, Norman Eugene;

Almstead, Neil

Gregory; Laughlin, Steven Karl; Natchus,

Michael

George; De, Biswanath

PATENT ASSIGNEE(S):

USA

SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part
of Appl.

PCT/US01/08783.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

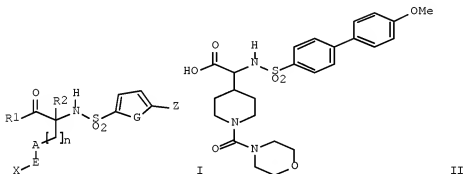
English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20030171400	A1	20030911	US 2002-246201	
20020918 <--				
WO 2001070690	A1	20010927	WO 2001-US8783	
20010320 <--				
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GH, GM,	HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,			
LR, LS,	LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,			

PT, RO,
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 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
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 PRIORITY APPLN. INFO.: US 2000-191303P P
 20000321 <-- WO 2001-US8783 A2
 20010320 <--
 OTHER SOURCE(S): MARPAT 139:245903
 GI



AB The title compds. [I; R1 = OH, NHOH; R2 = H, alkyl, haloalkyl, etc.; A = (un)substituted monocyclic heterocycloalkyl; A can be connected to R2 to form (un)substituted monocyclic heterocycloalkyl; n = 0-4; E = a bond, alkyl, CO, etc.; X = H, alkyl, aryl, etc.; G = S, O, N:N, etc.; Z = cycloalkyl, heterocycloalkyl, etc.] such as II which are inhibitors of metalloproteases and which are effective in treating conditions characterized by excess activity of these enzymes such as arthritis and cancer, were claimed and formulated (prepn. are given but no data are given for intermediates and final compds.).

=> d 19 ibib abs 6-12

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:570642 CAPLUS Full-text
 DOCUMENT NUMBER: 139:117342
 TITLE: Preparation of
 biphenylsulfonamidoheterocyclylcarboxylates as
 metalloprotease inhibitors
 INVENTOR(S): Pikul, Stanislaw; Ohler, Norman Eugene;
 Almstead, Neil

Gregory; Laughlin, Steven Karl; Natchus,

George; De, Biswanath; Hershberger, Paul

The Procter & Gamble Company, USA

U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part

No. PCT/US01/08931.

CODEN: USXXCO

Patent

English

2

$$\text{XEA}(\text{CH}_2)_n\text{C}(\text{R}^1)(\text{R}^2)\text{N}^3\text{G}_2\text{G}_1\text{M}_2$$

AB Title compds. [I; R1 = OH, NHOH; R2 = H, alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkylalkyl, heterocycloalkylalkyl, aralkyl, heteroaralkyl; R3 = alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, (hetero)cycloalkyl, aralkyl, heteroarylalkyl; A = (substituted) monocyclic heterocycloalkyl having 3-8 ring atoms of which 1-3 are heteroatoms; a, n = 0-4; E = bond, alkyl, CO, CO2, CONR4, SO2, CSNR4; R4 = H, alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl; X = H, alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, (hetero)cycloalkyl; G = S, O, NR5, CR5:CR5', N:CR5, N:N; R5, R5' = H, alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, (hetero)cycloalkyl; G1 = S, O, NR6, CR6:CR6', N:CR6, N:N; R6, R6' = H, alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; M = CH, N; Z = (CR7R7')aLR8; R7, R7' = H, alkyl, alkenyl, alkynyl, aryl, heteroalkyl, heteroaryl, (hetero)cycloalkyl, halo, haloalkyl, OH, alkoxy; L = bond, O, SOb, CO, CONR9, NR9, NR9CO; b = 0-2; R9 = H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalkyl, heteroaryl, (hetero)cycloalkyl, haloalkyl; AR2, XR4, R7R9, R8R9 = atoms to form a (substituted) heterocyclic ring containing 5-8 atoms of which 1-3 are heteroatoms; R8 = H, alkyl, alkenyl, alkynyl, halo, heteroalkyl, haloalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, are claimed. No synthetic or biol. data is given.

L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2009 ACS on STM

ACCESSION NUMBER: 2003:511339 CAPLUS Full-text
DOCUMENT NUMBER: 139:85328
TITLE: Preparation of tetracyclic heterocycles as selective estrogen receptor modulators (SERMs).
INVENTOR(S): Kanojia, Ramesh M.; Jain, Nareshkumar F.; Ng, Raymond;
PATENT ASSIGNEE(S): Sui, Zhihua; Xu, Jiayi
SOURCE: Ortho-McNeil Pharmaceutical, Inc., USA
PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053977	A1	20030703	WO 2002-US38486	
20021202 <--				
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 CA 2471107 A1 20030703 CA 2002-2471107
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 AU 2002362041 A1 20030709 AU 2002-362041
 20021202 <--
 BR 2002015152 A 20041019 BR 2002-15152
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 EP 1467998 A1 20041020 EP 2002-797167
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 EP 1467998 B1 20060329
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 JP 2005513133 T 20050512 JP 2003-554693
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 CN 1620457 A 20050525 CN 2002-828144
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 HU 2005000103 A2 20050530 HU 2005-103
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 HU 2005000103 A3 20090128
 AT 321764 T 20060415 AT 2002-797167
 20021202 <--
 PT 1467998 T 20060831 PT 2002-797167
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 ES 2264737 T3 20070116 ES 2002-797167
 20021202 <--
 NZ 533281 A 20070531 NZ 2002-533281
 20021202 <--
 RU 2305099 C2 20070827 RU 2004-118606
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 IN 2004KN00833 A 20060421 IN 2004-KN833
 20040616 <--
 MX 2004006034 A 20050331 MX 2004-6034
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 ZA 2004005653 A 20060628 ZA 2004-5653
 20040715 <--
 HK 1068875 A1 20060922 HK 2005-101213
 20050215 <--
 PRIORITY APPLN. INFO.: US 2001-341957P P
 20011219 <-- WO 2002-US38486 W
 20021202 <--
 OTHER SOURCE(S): MARPAT 139:85328
 GI

J.
 PATENT ASSIGNEE(S): Pharmacia Corp., USA
 SOURCE: U.S. Pat. Appl. Publ., 99 pp., Cont. of U.S.
 Ser. No.

570,731.
 CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20030073718	A1	20030417	US 2001-989943	
20011121 <--				
US 6683093	B2	20040127		
US 6750228	B1	20040615	US 2000-570731	
20000512 <--				
CA 2467565	A1	20030605	CA 2002-2467565	
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WO 2003045944	A1	20030605	WO 2002-US37093	
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AU 2002352795	A1	20030610	AU 2002-352795	
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BR 2002014450	A	20040914	BR 2002-14450	
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EP 1472244	A1	20041103	EP 2002-789749	
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JP 2005514375	T	20050519	JP 2003-547394	
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US 20040209914	A1	20041021	US 2003-730403	
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PRIORITY APPLN. INFO.:			US 2000-570731	A2

20000512 <--	US 1997-66007P	P
19971114 <--	US 1998-95347P	P
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19980918 <--	US 1999-256948	B2
19990224 <--	US 1999-311837	A2
19990514 <--	US 2001-989943	A
20011121 <--	WO 2002-US37093	W
20021119 <--		
OTHER SOURCE(S):	MARPAT 138:321016	
GI		

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE
PRINT *

AB Title compds. I [Z = C(O), O, S, NR6, etc.; R6 = H, CHO, sulfonyl, etc.; E = bond, C(O), S; Y = H, alkyl, alkoxy, haloalkyl, aryl, etc.; R = H, CN, perfluoroalkyl, trifluoromethoxy, etc.] are prepared. For instance, Me chloroacetate is reacted with p-fluorothiophenol and the resulting sulfide oxidized to the sulfone (MeOHag, Oxone), reacted with bis(2-bromoethyl)ether (DMAC, K2CO3, DMAP, Bu4NBr), saponified (THF, KOTMS) and coupled to a solid support to give II [P = polymer support]. II is reacted with Et isonipecotate (NMP, 80°, 65 h), the product saponified (dioxane, KOH), coupled with 3,5-dimethylpiperidine and released from the resin to give hydroxamic acid III. Example compds. are tested for inhibition of MMP-13, MMP-2 and MMP-1. I are useful for disorders associated with MMP and/or aggrecanase activity.

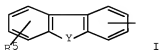
L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:137181 CAPLUS Full-text
 DOCUMENT NUMBER: 134:178144
 TITLE: Preparation of sulfonamido- and sulfinamido-
 containing carboxylic and hydroxamic acids derived from
 α,α' -disubstituted amino acids useful as
 matrix metalloproteinase inhibitors
 INVENTOR(S): Conrad, Christopher Alan; O'Brien, Patrick
 Michael;
 Ortwine, Daniel Fred; Picard, Joseph Armand;
 Sliskovic, Drago Robert
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA
 SOURCE: PCT Int. Appl., 70 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

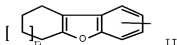
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012592	A2	20010222	WO 2000-US21884	
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WO 2001012592	A3	20010705		
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CA 2378332	A1	20010222	CA 2000-2378332	
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EP 1210326	A2	20020605	EP 2000-955435	
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EP 1210326	B1	20040225		
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TR 200200410	T2	20020621	TR 2002-410	
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TR 200202165	T2	20021121	TR 2002-2165	
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TR 200202211	T2	20021121	TR 2002-2211	
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JP 2003507362	T	20030225	JP 2001-516893	
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AT 260251	T	20040315	AT 2000-955435	
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PT 1210326	T	20040730	PT 2000-955435	
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ES 2216938	T3	20041101	ES 2000-955435	
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MX 2001013324	A	20020702	MX 2001-13324	
20011219 <--				
US 6677355	B1	20040113	US 2002-49544	
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PRIORITY APPLN. INFO.:			US 1999-149660P	P
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OTHER SOURCE(S):
GI

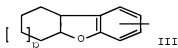
MARPAT 134:178144



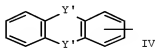
I



II



III



IV

AB R1S(O)dNR2CR3R4C(O)X (I; e.g. 1-(dibenzofuran-3-sulfonylamino)cyclohexanecarboxylic acid) or a pharmaceutically acceptable salt thereof are useful for inhibiting matrix metalloproteinase enzymes in animals, and as such, prevent and treat diseases resulting from the breakdown of connective tissues. In I, X = OH, NHOH; R1 = II, III, IV, 4-ArMpiperidino, 4-Arppiperazino, 4-(N-(4-R5phenyl)-4-piperidinyl)phenyl, 4-(4-R5phenyl)piperazinophenyl, V; Y = O, S, -S(O)d (d = 1, 2), CH2, C(O), and NRq (Rq = H, C1-6 alkyl, or C1-6 alkylphenyl); each Y' = O, S, SO2, CH2, C(O), and NH; M = O, S, CH2; R5 = H, C1-10 alkyl, CF3, CONH2, halo, CN, COOH, C1-4 alkoxy, CHO, NO2, OH, (CH2)pOH, (CH2)pNH2, Ar, and NH2; p = 0-3; Ar = (a) phenyl; (b) Ph substituted with C1-4 alkyl, C, C1-4 alkoxy, halo, NH2, NO2, CN, COOH, CONH2, CF3, or COOR6 (R6 = C1-10 alkyl); and (c) heteroaryl; R2 = (a) H; (b) C1-4 alkyl; (c) benzyl; and (d) benzyl substituted with ≥ 1 C1-4 alkyl, C1-4 alkoxy, F, Cl, Br, I, NH2, NO2, CN, carboxy, and CO2R7 (R7 = H or C1-4 alkyl); and R3 and R4 are either (1) C1-20 alkyl; C3-10 cycloalkyl; phenyl; Ph substituted with C1-4 alkyl, C1-4 alkoxy, halo, NH2, NO2, CN, COOH, CO2R7, or CF3; C3-10 heterocyclic; and heteroaryl; or (2) substituents taken together to form a group of the empirical formula $-(CH_2)_sZg-$, wherein said substituents form a ring including the carbon atom adjacent the carbonyl group in I, and wherein s = 2-10; g = 0-6; and each Z is located at any position of said substituents and each Z = O, S, and NR8 (R8 = H, C1-3 alkyl). Also disclosed are pharmaceutical compns. and methods of treating diseases in which matrix metalloproteinases are involved including multiple sclerosis, atherosclerotic plaque rupture, restenosis, aortic aneurysm, heart failure, periodontal disease, corneal ulceration, burns, decubital ulcers, chronic ulcers or wounds, cancer metastasis, tumor angiogenesis, osteoporosis, rheumatoid or osteoarthritis, renal disease, left ventricular dilation, or other autoimmune or inflammatory diseases dependent upon tissue invasion by leukocytes. Other diseases for which I are claimed effective are: stroke, head trauma, spinal cord injury, Alzheimer's disease, amyotrophic lateral sclerosis, cerebral amyloid angiopathy, AIDS, Parkinson's disease, Huntington's disease, prion diseases, myasthenia gravis, and Duchenne's muscular dystrophy. Results of measurement of IC50 for matrix metalloproteinase enzyme inhibition

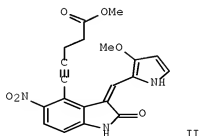
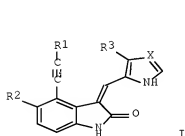
are presented for 7 examples of I. Although the methods of preparation are not claimed, 33 example preps. are included.
 REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2000:421131 CAPLUS Full-text
 DOCUMENT NUMBER: 133:43432
 TITLE: Preparation of
 4-alkynyl-3-(pyrrolylmethylene)-2-oxoindoles
 as
 inhibitors of cyclin-dependent kinases, in
 particular
 CDK2
 INVENTOR(S): Chen, Yi; Corbett, Wendy Lea; Dermatakis,
 Apostolos;
 Liu, Jin-jun; Luk, Kin-chun; Mahaney, Paige
 E.;
 Mischke, Steven Gregory
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
 SOURCE: PCT Int. Appl., 170 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035908	A1	20000622	WO 1999-EP9624	
19991208 <--				
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2354873	A1	20000622	CA 1999-2354873	
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BR 9916327	A	20010918	BR 1999-16327	
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EP 1157019	A1	20011128	EP 1999-963422	
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TR 200101860	T2	20011221	TR 2001-1860	
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JP 2002532492	T	20021002	JP 2000-588168	
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AT 234830	T	20030415	AT 1999-963422	
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ES 2192877	T3	20031016	ES 1999-963422	
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CN 1138773	C	20040218	CN 1999-814524	
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AU 770375	B2	20040219	AU 2000-19727	
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US 6130239	A	20001010	US 1999-464502	
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US 6303793	B1	20011016	US 2000-566054	
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ZA 2001004275	A	20020826	ZA 2001-4275	
20010524 <--				
MX 2001005934	A	20010911	MX 2001-5934	
20010612 <--				
PRIORITY APPLN. INFO.:			US 1998-112591P	P
19981217 <--				
			US 1999-149073P	P
19990816 <--				
			WO 1999-EP9624	W
19991208 <--				
			US 1999-464502	A3
19991215 <--				
OTHER SOURCE(S):	MARPAT 133:43432			
GI				



AB The title compds. (I) [wherein R1 = H, acyl, carboxy, carbamido, (un)substituted (cyclo)alkyl, or heterocyclyl; R2 = H, alkoxy, acyl(oxy), carboxy, carbamido, halogen, NO2, CN, sulfamido, perfluoroalkyl, alkyl, etc.; R3 = H, alkoxy, acyl(oxy), carboxy,

carbamido, halogen, CN, amino, perfluoroalkyl, alkyl, etc.; X = N or (un)substituted C] and their intermediates and analogs were prepared by reaction of alkynes with 4-halo-2-oxindoles. I inhibit cyclin-dependent kinases (CDKs), especially CDK2, and are useful as anti-proliferative agents in the treatment or control of cell proliferative disorders, in particular breast and colon tumors. For example, Me 4-pentynoate was coupled with (Z)-4-bromo-1,3-dihydro-3-[(3-methoxy-1H-pyrrol-2-yl)methylene]-5-nitro-2H-indole-2-one (preparation given) using (Ph3P)2PdCl2 and CuI as catalysts in DMF and TEA to give (Z)-II in 72% yield. In a CDK2 flash plate assay, II inhibited CDK2 by > 90% at concns. of ≤ 1.0 μ M. Representative compds. of the invention were tested in cell-based assays against epithelial breast carcinoma line MDA-MB435 and colon carcinoma line SW480 and gave IC50 values of < 3.5 μ M and < 1.0 μ M, resp. Formulations for tablets, capsules, and injection solution/emulsion preps. are also included.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1954:11089 CAPLUS Full-text

DOCUMENT NUMBER: 48:11089

ORIGINAL REFERENCE NO.: 48:2058c-i,2059a-h

TITLE: Some reactions of 2-alkoxy -3,4-dihydro-2H-pyrans

AUTHOR(S): Longley, Raymond I., Jr.; Emerson, Wm. S.; Shafer,

Theodore C.

CORPORATE SOURCE: Monsanto Chem. Co., Dayton, O.

SOURCE: Journal of the American Chemical Society (1952), 74, 2012-15

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 48:11089

AB cf. C.A. 44, 10705b. 2-Alkoxy-3,4-dihydro-2H-pyrans were hydrogenated to 2-alkoxytetrahydropyrans and hydrogenolyzed to 5-alkoxypentanol. The dihydropyrans were converted to 1,5-pentanedioles by hydrolysis and hydrogenation in both 1- and 2-step operations. The diols were dehydrogenated to δ -lactones by both liquid- and vapor-phase procedures. δ -Lactones were prepared by treating the corresponding dialdehydes with aqueous alkali. The δ -lactones with NH3 yielded piperidones, which were alkylated and vinylated. 2-Ethoxy-3,4-dihydro-2H-pyran (I) (150 g.) and 13 g. Raney Ni heated to 70°, the bomb shaken 1 hr. at 125° under H at 1200 lb./sq. in., the mixture filtered, and distilled, yielded 117 g. 2-ethoxytetrahydropyran (II) b. 136°, n25D 1.4238. The 2-MeO isomer (III) yielded 92% 2-methoxytetrahydropyran (IV), b. 123-6°, n25D 1.4223-7. I (160 g.) and 11 g. Cu chromite under 1000 lb./sq. in. H pressure heated rapidly to 200°, the temperature raised slowly to 250° at 1600 lb./sq. in. and held there 4 hrs., and the filtered mixture distilled yielded 33 g. EtOH and tetrahydropyran (V), 63 g. crude 2-ethoxytetrahydropyran, b760 77°, b20 50°, n25D 1.4212; 4 g. intermediate; and 21 g. 5-

ethoxypentanol, b14 94-7°, b9 88-91°, n25D 1.4277, b14-15 98°, n25D 1.4288. The 2-BuO homolog (140 g.) and 6 g. Cu chromite heated rapidly to 255° at 1700 lb./sq. in. and held there 3 hrs. yielded 19 g. crude V, b. 80-100°; 22 g. crude BuOH b760 100°, b12 35°; 19 g. intermediate, 31 g. 2-butoxytetrahydropyran, b12 70-2°, n25D 1.4294; 6 g. intermediate; and 27 g. 5-butoxypentanol, b12 115-18°, n25D 1.4334, b9-10 108°, n25D 1.4342. 2-Methoxy-4-methyl-3,4-dihydro-2H-pyran (425 g.), 800 cc. water, and 30 cc. HCl stirred 2 hrs. at 24-42°, the mixture neutralized with NaHCO3, a 1004-g. portion and 39 g. Raney Ni shaken 4 hrs. under 1625 lb./sq. in. H pressure at 125°, filtered, and distilled, yielded 281 g. 3-methyl-1,5-pentanediol (VA), b17 139-46°, n25D 1.4518. 2-Ethoxy-4-furyl-3,4-dihydro-2H-pyran (100 g.) in 200 cc. MeOH, 50 cc. water, and 5 cc. HCl hydrolyzed at 50°, neutralized with 6 g. NaHCO3, hydrogenated 2.5 hrs. at 140-60° and 600-1700 lb./sq. in. over 24 g. Raney Ni, yielded 53 g. 3-furyl-1,5-pentanediol, b5 173°, n25D 1.4843, d2525 1.088.

2-Ethoxy-4-phenyl-3,4-dihydro-2H-pyran (102 g.), 300 cc. dioxane, 45 cc. water, and 10 cc. HCl heated to 60°, the mixture let stand 1 hr. at 60-45°, treated with 11 g. NaHCO3, and the upper layer distilled, yielded 31 g. 3-phenylglutaraldehyde (VI), b0.6 140-2°, n25D 1.5484. VI (9 g.) and 1 g. water let stand several days yielded 6.5 g. 2,6-dihydroxy-4-phenyltetrahydropyran, m. 102-4°.

2-Methoxy-4-methyl-3,4-dihydro-2H-pyran (VII) (325 g.), 100 cc. water, and 40 g. Cu chromite shaken 7 hrs. at 180° and 2800 lb./sq. in., yielded 268 g. VA, b5 103°, b1.5 106°, n25D 1.4515. The preceding experiment at 1500-2250 lb./sq. in. 4 hrs. at 180° and 45 min. at 210° yielded 10 g. forerun, 29 g. β-methyl-δ-valerolactone, b2 72°, n25D 1.4496; 10 g. intermediate; and 113 g. VA, b2 106°. VII (350 g.) hydrogenated 6 hrs. in 100 cc. water over 40 g. Ni-kieselguhr at 160-235° and 1200-200 lb./sq. in. yielded 17 g. forerun, and 229 g. VA, b3 109.5°, n25D 1.4525; dibenzoate, b0.1 174°, n25D 1.5371, d2525 1.110. III (325 g.), 100 cc. water, and 40 g. Cu chromite hydrogenated 7.5 hrs. at 165-80° and 1400 2250 lb./sq. in. yielded 257 g. 1,5-pentanediol, b19 141°, b20 144°, n25D 1.4462-82. Acrolein (60 g.) and 100 cc. EtCH:CHOMe heated 16 hrs. at 160° yielded 105 g. 2-methoxy-3-ethyl-3,4-dihydro-2H-pyran (VIII), b13 51°, n25D 1.4420, d2525 0.962. VIII (102 g.) in 25 cc. water containing 12 g. Cu chromite hydrogenated 2 hrs. at 240-60° and 2600-4000 lb./sq. in. yielded 71 g. 2-ethyl-1,5-pentanediol, b11 143-6°, n25D 1.4567, d2525 0.967. VIII (353 g.), 100 cc. water, and 30 g. Cu chromite shaken 5 hrs. at 200° yielded 35.5 g. forerun, and 163.5 g. β-methyl-δ-valerolactone (IX), b14 107°, n25D 1.4493-1.4496. N passed 12 hrs. over pumice impregnated with basic Cu carbonate at 100°, H passed through 24 hrs. at 200°, 150 g. VA added dropwise with H continued at 240° during 3 hrs., and the product distilled yielded 130 g. IX, b14 107°, n25D 1.4495-1.4498, d2525 1.044. VA (197 g.) and 10 g. Cu chromite stirred 90 min. at 190-205° yielded 180 g. VIII, b15 110-11°, n25D 1.4495. VII (493 g.), 900 cc. water, and 30 cc. concentrated HCl stirred 70 min., cooled, 200 g. NaOH in 800 cc. water added over 5 hrs. (temperature held below 45°), the mixture stirred 1.5 hrs., let stand overnight, and extracted with Et2O yielded (probably) 42 g. 2,6-dimethoxy-4-methyltetrahydropyran, b20 76-8°, n25D 1.4252, d2525 0.983; the aqueous layer on acidification with 420 cc. HCl and extraction

with Et₂O yielded 232 g. VIII, b₂₀ 116-17°. III (400 g.), 600 cc. water, and 20 cc. HCl stirred 1 hr., the solution added during 2 hrs. to 187 g. NaOH in 1500 cc. water at 25-35°, the mixture stirred 16 hrs. at 25-35°, saturated with NaCl, extracted with Et₂O, and the exts. distilled yielded 22 g. (probably) 2,6-dimethoxytetrahydropyran (IXA), b₂₁ 65-7°, n_{25D} 1.4262, d₂₅₂₅ 1.013. IXA (1.5 g.) and 3 cc. 4% HCl heated to boiling, cooled, saturated with NaHCO₃. treated with 3 g. HONH₂.HCl, kept alkaline with NaHCO₃ and diluted with water, yielded glutaraldehyde dioxime, m. 165-7°. The aqueous layer with 400 cc. HCl and 56 hrs. continuous extraction with Et₂O yielded 190 g. δ-valerolactone (X), b₂₂ 112-16°; n_{25D} 1.4546-73. VI (57 g.) in 80 cc. Et₂O added to 13 g. NaOH in 150 cc. water during 10 min., the mixture stirred 1 hr., let stand overnight, the aqueous layer treated with 30 cc. concentrated HCl, extracted with 100 cc. C₆H₆, the organic layers combined and distilled yielded 29 g. β-phenyl-δ-valerolactone, b_{0.4} 135°, n_{25D} 1.5475, d₂₅₂₅ 1.150; distillation of the Et₂O layer yielded 15 g. (probably) 2,6-diethoxy-4-phenyltetrahydropyran, b_{1.0} 143-6°, n_{25D} 1.4980, d₂₅₂₅ 1.035. X (430 g.) and 100 g. NH₃ heated 15 hrs. at 230°, excess NH₃ vented, and the product and C₆H₆ rinsings distilled, yielded 106 g. X, 254 g. 2-piperidone (XI), b₂₃ 147-50° (decomposition), 15 g. liquid b₁₀ about 80°, and 47 g. residue. IX (644 g.) and 130 g. NH₃ rocked 13 hrs. at 230°, the NH₃ evaporated, the product cooled to 45°, and distilled, yielded 5 g. forerun, 153 g. IX, b₃ 105-42°, 445 g. 4-methyl-2-piperidone (XII), b₁₃ 143-5°, and 25 g. residue. XII m. 88-91°. 4-(2-Aminoethyl)morpholine (65 g.), 60 g. IX, and 40 cc. C₆H₆ refluxed 22 hrs. at 240° (water trap) yielded 10 g. forerun, b₁₂ 102-35°, n_{25D} 1.4552; 71 g. 1-(2-morpholinoethyl)-4-methyl-2-piperidone, b₁ 150-1°, n_{25D} 1.4953. XII (113 g.) in 100 cc. xylene added slowly (temperature held below 70°) to 26 g. NaH in 200 g. xylene under N, the mixture stirred 30 min. at 60-70°, warmed to 90°, 135 g. CH₂:CMeCH₂Br added at 90-100°, the mixture stirred 1 hr. at 90-100°, filtered warm and distilled, yielded 70 g. 1-methyl-4-methyl-2-piperidone, b_{0.5} 80°, n_{25D} 1.4834. About 1 g. K in molten XI shaken 2 hrs. at 155° under 255 lb./sq. in. pressure of C₂H₂, and the product flash distilled yielded 63 g. 1-vinyl-2-piperidone b₂₅ 125-6°, m. 42-8°. K (1 g.) and 150 g. XII yielded 49 g. 4-methyl-1-vinyl-2-piperidone, b₁₂ 113-14° n_{25D} 1.5040, d₂₄₂₅ 1.006.

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1951:38734 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 45:38734

ORIGINAL REFERENCE NO.: 45:6633f-i,6634a-b

TITLE: Some derivatives of tetrahydropyran as potential

pharmacodynamic agents. II

AUTHOR(S): Burger, Alfred; Turnbull, Lennox B.; Dinwiddie, J.

Gray, Jr.

CORPORATE SOURCE: Univ. of Virginia, Charlottesville

SOURCE: Journal of the American Chemical Society (1950), 72, 5512-15

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE:

Journal

LANGUAGE:

Unavailable

AB

cf. C.A. 37, 2372.8. Reduction of 77.5 g. 4-carboxytetrahydropyran with AlLiH_4 in Et_2O gave 23.4 g. tetrahydro-4-pyranmethanol, b20 105-10°, n28D 1.460 (phenylurethane, m. 86.5-88°), which with PBr_3 in CCl_3 below 0° yielded 34.6% 4-(bromomethyl)tetrahydropyran, b20 84-6°, n28D 1.4918 [4-(2-naphthoxy Me analog, m. 70-2°] which with $\text{NaCMe}(\text{CO}_2\text{Et})_2$ gave 65.5% di-Et methyl(tetrahydro-4-pyranylmethyl)malonate, b0.5 134-7°, yielding on hydrolysis and decarboxylation 77% α -methyl-tetrahydro-4-pyranpropionic acid, b0.5 130-5° m. 37-43°, which with SOCl_2 formed 90% of the acid chloride, b0.5 85°, degraded by the Curtius method to 81% 1-(tetrahydro-4-pyranyl)-2-aminopropane, b20 89°. 4-Phenyl-4-acetyltetrahydropyran (I), m. 59.5-60.5°, b2 133-41°, obtained in 64% yield from the CN compound and MeMgI , was brominated in CCl_4 to yield 59% 4-phenyl-4-(dibromoacetyl)tetrahydropyran (II), m. 97-8°. Refluxing I with HCO_2NH_4 and hydrolysis of the product gave 67% 1-(4-phenyltetrahydro-4-pyranyl)ethylamine-HCl, m. 241-3° (N-Bz derivative, m. 129-30°). Similarly I and AcONH_4 gave 14% 1-(4-phenyltetrahydro-4-pyranyl)-N-methylethylamine-HCl, m. 267.5-68.5°. Addition of CH_2N_2 to tetrahydro-4-phenyl-4-pyrancarbonyl chloride and reaction of the product with aqueous HBr gave 87% 4-phenyl-4-(bromoacetyl)tetrahydropyran (III), m. 48.5-9.5°, reduced by the Meerwein method to 72% 1-(4-phenyltetrahydro-4-pyranyl)-2-bromoethanol (IV), m. 103.5-4.5°, which with alc. KOH gave 62% of 4-phenyl-4-ethyleneoxytetrahydropyran (V), b0.8 125-30°; this, refluxed with morpholine, gave 1-(4-phenyltetrahydro-4-pyranyl)-2-(4-morpholinyl)ethanol, b0.5 158-60° (HCl salt, m. 210-11.5°), also obtained by condensation of III with morpholine to 4-phenyl-4-(4-morpholinylacetyl)tetrahydropyran diliturate, decomposition 220.3°, and reduction of the latter with $(\text{Me}_2\text{CHO})_3\text{Al}$. By condensation of the appropriate secondary amine with III and reduction of the product or by condensation of the amines with IV or V were also obtained 4-phenyl-4-(diethylaminoacetyl)tetrahydropyran diliturate, m. 209.5-13.5°, 4-phenyl-4-(1-piperidylacetyl)tetrahydropyran diliturate, m. 205-6°, 37% α -(4-phenyl-4-tetrahydropyranyl)-1-pyridineethanol-HCl (VI), m. 224-7°, and 20% 1-(4-phenyltetrahydro-4-pyranyl)-2-dipropylaminoethanol-HCl (VII), m. 157-65°. Attempts to brominate I to III persistently gave II. Neither VI nor VII exhibited analgetic, topical anesthetic, or antihistaminic activities. Both caused coronary constriction in the rabbit and VII caused cardiac depression similarly to khellin.